



İlaç Direnci: Korkalım mı?

Mert Ahmet Kuşkucu PhD

Prof. Dr. Kenan Midilli

İ.Ü. Cerrahpaşa Tıp Fakültesi

Tıbbi Mikrobiyoloji Anabilim Dalı

2016 sonu

HIV ile infekte kiři sayısı: 36.7 milyon

Tanı konma oranı: %70

Tanı konanlar arasında tedavi alma oranı %77

Tedavi alanlar arasında baskılanma oranı %82

Temmuz 2017 ART alan kiři sayısı: 20.9 milyon

HIVDR varsa:

- Olumsuz tedavi sonlanımları
- Artmış mortalite
- Uygulanan tedavi rejimlerinin sürdürülebilirlik ve etkililiğinde azalma
- NNRTI PDR'ı olan ve NNRTI içeren tedavi alanlarda virolojik baskılanma olasılığı düşük; ölüm ya da virolojik başarısızlık olasılığı 23 kat fazla; tedaviyi yarıda bırakma olasılığı da 9 kat yüksek

Tedaviye yeni başlayan ya da yeniden başlayanlarda ilaç direnci > %10 olursa ve NNRTI bazlı tedavilere devam edilecek olursa sadece Sahraaltı Afrika'da 2016-2030 arasında doğurabileceği tahmini sonuçlar:

- AIDS'e bağlı 890 000 ölüm
- 450 000 yeni HIV enfeksiyonu

Düşük ve Orta Gelir Düzeyi Ülkelerde

DSÖ 2010 : NNRT direnci %5.5

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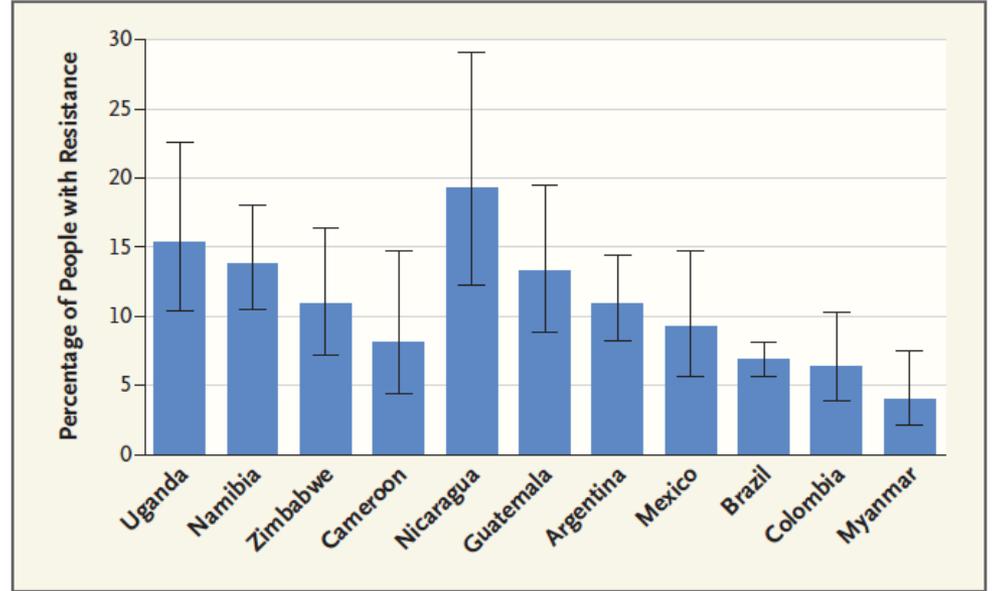
İlk kez tedaviye başlayan tedavi deneyimsiz kişilerde: NNRTI direnci > %10

Tedaviye yeniden başlayan daha önce tedavi başlanmış kişilerde ise > %20

DSÖ tedavi önerisi:

1 NNRTI (Efavirens) + 2 NRTI (tenefovir artı Lamivudin ya da emtrisitabin)

2015'te yapılan meta-analiz ve sistematik derlemelere göre bu ülkelerde tedaviye başlayan erişkinlerin %20'sinde 16-60 ayın sonunda viral baskılanma elde



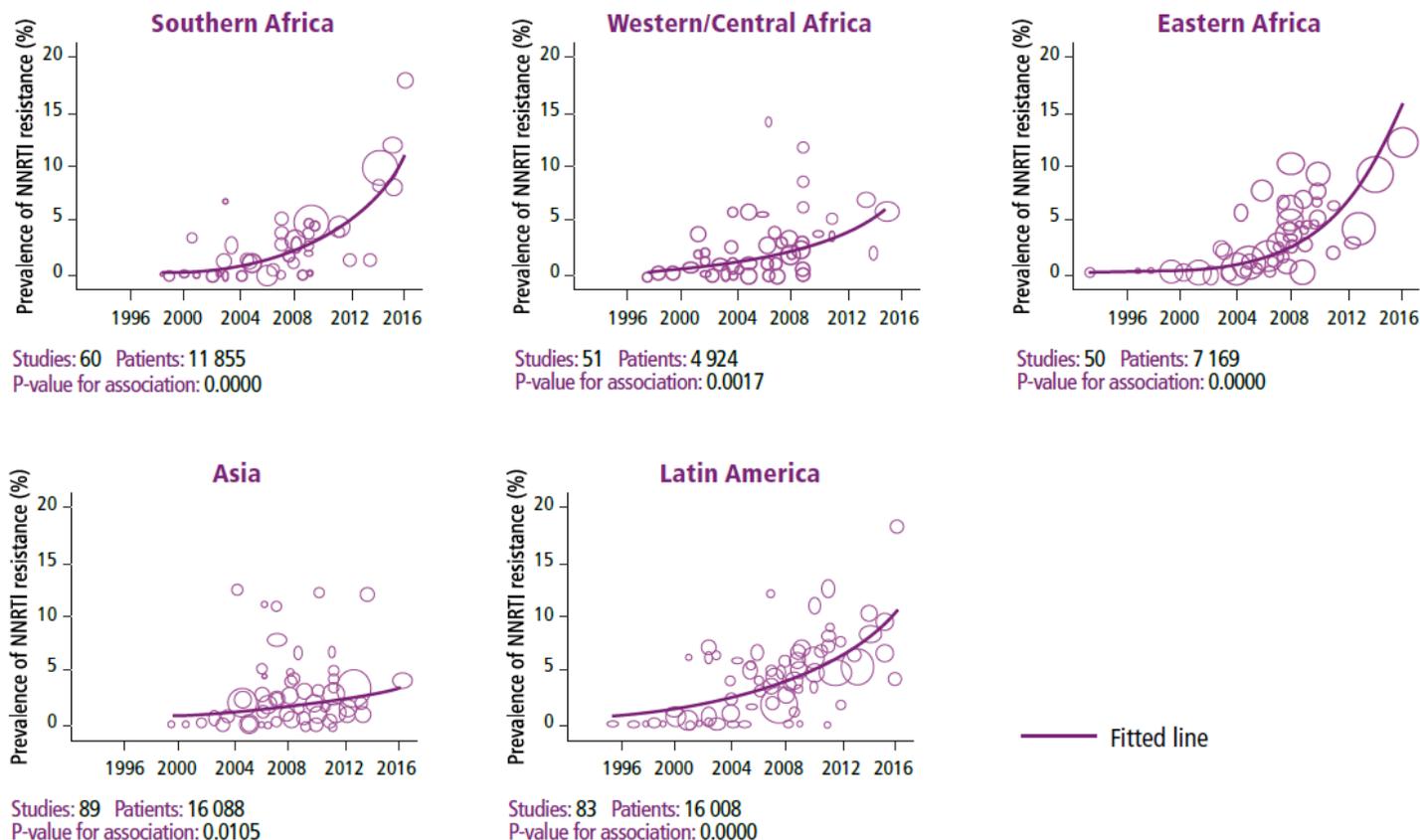
Pretreatment HIV Drug Resistance to Nonnucleoside Reverse Transcriptase Inhibitors in 11 Countries.

HIV-1 drug resistance before initiation or re-initiation of first-line antiretroviral therapy in low-income and middle-income countries: a systematic review and meta-regression analysis

Ravindra K Gupta, John Gregson, Neil Parkin, Hiwot Haile-Selassie, Amilcar Tanuri, Liliana Andrade Forero, Pontiano Kaleebu, Christine Watera, Avelin Aghokeng, Nicholus Mutenda, Janet Dzangare, San Hone, Zaw Zaw Hang, Judith Garcia, Zully Garcia, Paola Marchorro, Enrique Beteta, Amalia Giron, Raph Hamers, Seth Inzaule, Lisa M Frenkel, Michael H Chung, Tulio de Oliveira, Deenan Pillay, Kogie Naidoo, Ayesha Kharsany, Ruthiran Kugathasan, Teresa Cutino, Gillian Hunt, Santiago Avila Rios, Meg Doherty, Michael R Jordan, Silvia Bertagnolio

***Lancet Infect Dis* 2017, S1473-3099(17)30702-8**

Fig. 7: Prevalence of NNRTI pretreatment resistance by calendar year across studies included in the systematic review



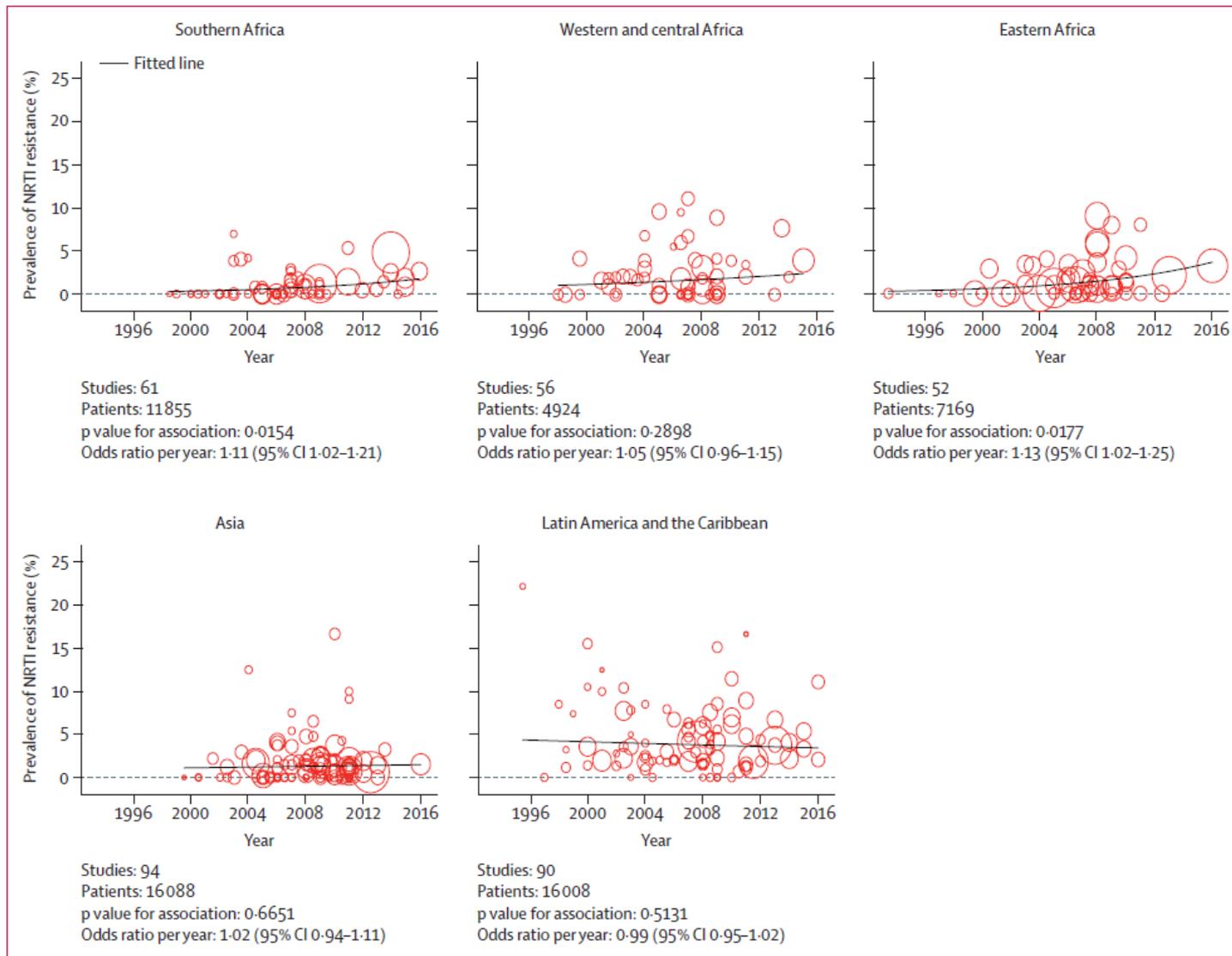


Figure 2: Prevalence of pretreatment HIV resistance to NRTI by year of sampling

	FIRST 90				SECOND 90				THIRD 90			
	Knowledge of status among all people living with HIV *	Is community-based testing and counselling and/or by provider testing available?	Is self-testing available?	Is assisted partner notification available?	Percentage of people living with HIV who know their status who are on treatment*	Percentage of all people living with HIV who are on treatment*	Recommended antiretroviral treatment initiation threshold among people living with HIV per Ministry of Health guidelines	Is antiretroviral therapy provided in community settings (such as outside health facilities) for people who are stable on antiretroviral therapy in your country?	Percentage of people living with HIV on treatment who are virally suppressed*	Percentage of all people living with HIV who are virally suppressed*	Is there a national policy on routine viral load testing for adults and adolescents?	Percentage of people living with HIV on antiretroviral therapy who received a viral load test
ANDORRA												
AUSTRIA ^{1,2,3}	88%				85%	75%			76%	57%		
BELGIUM ^{1,2,3}	84%				84%	71%			>89%	67%		
BULGARIA ^{1,2,3}	64%				36%	23%			87%	20%		
CANADA ^{1,2}	80%				76%	61%			89%	54%		
CROATIA												
CYPRUS												
CZECHIA	75%				69%	52%			>89%	50%		
DENMARK ¹	89%				89%	81%			89%	72%		

SWITZERLAND^{1,3}	82%						>89%	75%			>89%	72%
TURKEY												
UNITED KINGDOM^{1,2,3}	87%						>89%	>81%			>89%	78%
UNITED STATES												

IRELAND	85%				>89%	77%						
ISRAEL ^{1,2,3}	74%				69%	51%						
ITALY ^{1,2,3}	88%				88%	78%			87%	67%		
LATVIA						26%						
LIECHTENSTEIN												
LITHUANIA	88%				26%	23%			74%	17%		
LUXEMBOURG ²	85%				88%	75%			>89%	68%		
MALTA ^{2,3}	75%				>89%	72%			86%	62%		
MONACO												
NETHERLANDS ^{1,2,3}	88%				88%	77%			>89%	72%		
NORWAY												
POLAND ^{2,3}	57%				63%	36%			>89%	32%		
PORTUGAL	76%				>89%	70%			88%	62%		
ROMANIA	89%				77%	68%			>89%	64%		
SAN MARINO												
SERBIA ^{2,3}	63%				66%	42%			>89%	40%		
SLOVAKIA	79%				74%	59%						
SLOVENIA						54%			83%	44%		
SPAIN ³	82%				>89%	75%			88%	66%		
SWEDEN ^{1,2,3}	>89%				>89%	>81%			>89%	>75%		
SWITZERLAND ^{1,3}	82%				>89%	75%			>89%	72%		
TURKEY												
UNITED KINGDOM ^{1,2,3}	87%				>89%	>81%			>89%	78%		
UNITED STATES												
WESTERN AND CENTRAL EUROPE AND NORTH AMERICA						78%						



TURKEY

THE HIV EPIDEMIC

	2005	2010	2016
New HIV infections
HIV incidence per 1000 population
AIDS-related deaths
People living with HIV

90-90-90

	2016	
People living with HIV who know their HIV status
People living with HIV who are on treatment
Adults living with HIV who are on treatment
People living with HIV who are virally suppressed

CHILDREN AND PREGNANT WOMEN

	2010	2016
New HIV infections—children
Children living with HIV who are on treatment
Coverage of pregnant women living with HIV accessing antiretroviral medicines

HIV COMORBIDITIES

Estimated number of incident TB cases among people living with HIV (2015)	<100 [<100-<200]
Proportion of people living with HIV with active TB in HIV care	..
Cervical cancer screening of women living with HIV	..

HIV PREVENTION

Knowledge of HIV prevention among young people (15-24)	..
Condom use at last higher-risk sex (with a non-marital, non-cohabiting partner)	..
Males	..
Females	..
Women aged 15-49 who have their demand for family planning satisfied with modern methods	..
Men aged 15-49 who are circumcised	Not applicable
Male circumcisions performed according to national standards (2016)	Not applicable
People on PrEP (2016)	..

STIGMA AND DISCRIMINATION

People who report having discriminatory attitudes towards people living with HIV	..
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POLICIES AND REGULATIONS

	2016
Community delivery of treatment	..

Laws or policies restricting entry, stay and residence of people living with HIV	..
Criminalization of transmission of, nondisclosure of, or exposure to HIV	..
Recommended CD4 level for treatment initiation	TREAT ALL

HIV EXPENDITURE

	2012
Total expenditure	US\$ 12 291 905
Domestic public expenditure	US\$ 12 291 905
Domestic private expenditure	..
International expenditure	..

KEY POPULATIONS

SEX WORKERS	
Estimated size of population	..
HIV prevalence	..
Know HIV status	..
Antiretroviral therapy coverage	..
Condom use	..
Condoms distributed to sex workers enrolled in prevention programmes (2016)	..
Coverage of HIV prevention programmes	..
Avoidance of services due to stigma and discrimination	..

PEOPLE WHO INJECT DRUGS

Estimated size of population	..
HIV prevalence	..
Know their HIV status	..
Antiretroviral therapy coverage	..
Condom use	..
Clean needle use at last injection	..
Needles and syringes distributed per person who injects (2016)	..
Coverage of HIV prevention programmes	..
Coverage of opioid substitution therapy (2016)	..
Naloxone available (2016)	..
Safe injection rooms available (2016)	..
Avoidance of services due to stigma and discrimination	..

GAY MEN AND OTHER MEN WHO HAVE SEX WITH MEN

Estimated size of population	..
HIV prevalence	..
Know their HIV status	..
Antiretroviral therapy coverage	..
Condom use	..
Condoms distributed to men who have sex with men in prevention programmes (2016)	..
Coverage of HIV prevention programmes	..
Avoidance of services due to stigma and discrimination	..

TRANSGENDER PEOPLE

Estimated size of population	..
HIV prevalence	..
Know their HIV status	..
Antiretroviral therapy coverage	..
Condom use	..
Coverage of HIV prevention programmes	..
Avoidance of services due to stigma and discrimination	..

PRISONERS

Estimated size of population	..
HIV prevalence	..
Antiretroviral therapy coverage	..
HIV prevention programmes in prisons (2016)	..

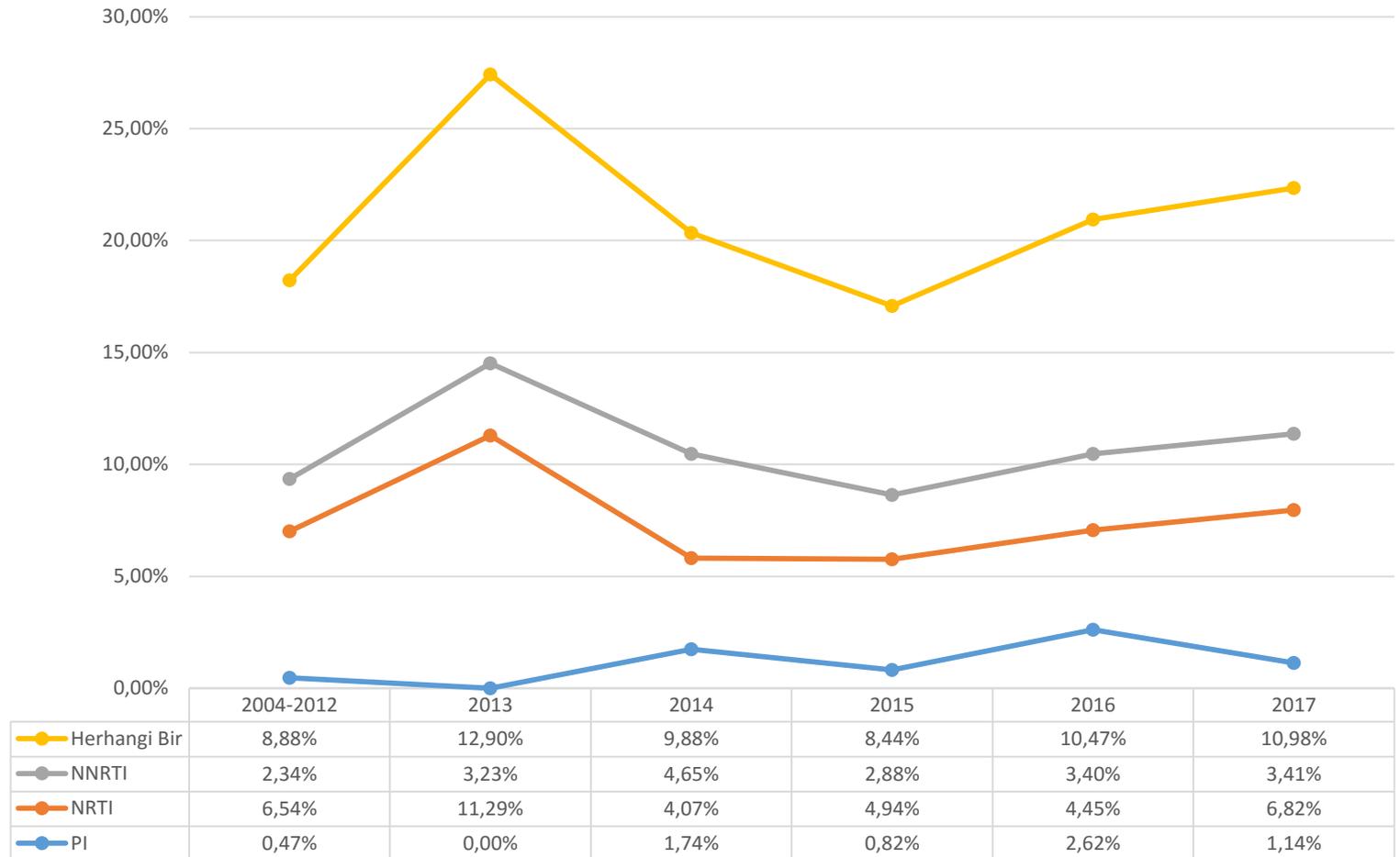
Drug Resistance Mutations for Surveillance of Transmitted HIV-1

Drug-Resistance: 2004-2017

Yıl	n (toplam 1580)	PI	NRTI	NNRTI	Herhangi Bir
2004-2012	214	1	14	5	19
		0.47%	6.54%	2.34%	8.88%
2013	62	0	7	2	8
		0.00%	11.29%	3.23%	12.90%
2014	172	3	7	8	17
		1.74%	4.07%	4.65%	9.88%
2015	486	4	24	14	41
		0.82%	4.94%	2.88%	8.44%
2016	382	10	17	13	40
		2.62%	4.45%	3.40%	10.47%
2017	264	3	18	9	29
		1.14%	6.82%	3.41%	10.98%
Toplam	1580	21	87	51	154
		1.33%	5.51%	3.23%	9.75%

Drug Resistance Mutations for Surveillance of Transmitted HIV-1

Drug-Resistance: 2004-2017 (total 1580)



Drug Resistance Mutations for Surveillance of Transmitted HIV-1

Drug-Resistance: 2016-2017

2016

M46	I50	G73	V82	N83	M41	D67	M184	T215	K219	K101	K103	V106	G190
PI					NRTI					NNRTI			
I, L	V, L	S, T, C, A	A, T, F, S, C, M, L	D	L	N, G, E	V, I	Y, F, I, S, C, D, V, E	Q, E, N, R	E, P	N, S	M, A	A, S, E
2	4	1	2	1	10	1	1	13	1	5	5	1	3
0.524%	1.047%	0.262%	0.524%	0.262%	2.618%	0.262%	0.262%	3.403%	0.262%	1.309%	1.309%	0.262%	0.785%

TAM1: M41L, L210W ve T215Y

TAM2: D67N, K70R, T215F ve K219Q/E

2017

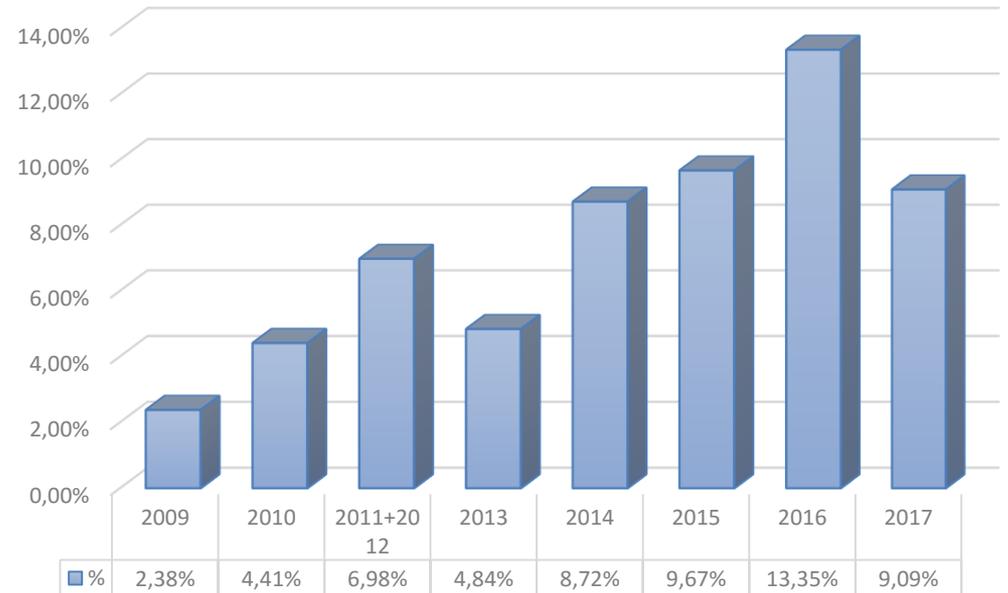
M46	I54	M41	D67	K70	M184	T215	K103	G190	P225
PI		NRTI					NNRTI		
I, L	V, L, M, A, T, S	L	N, G, E	R, E	V, I	Y, F, I, S, C, D, V, E	N, S	A, S, E	H
2	1	10	2	1	3	14	7	1	1
0.758%	0.379%	3.788%	0.758%	0.379%	1.136%	5.303%	2.652%	0.379%	0.379%

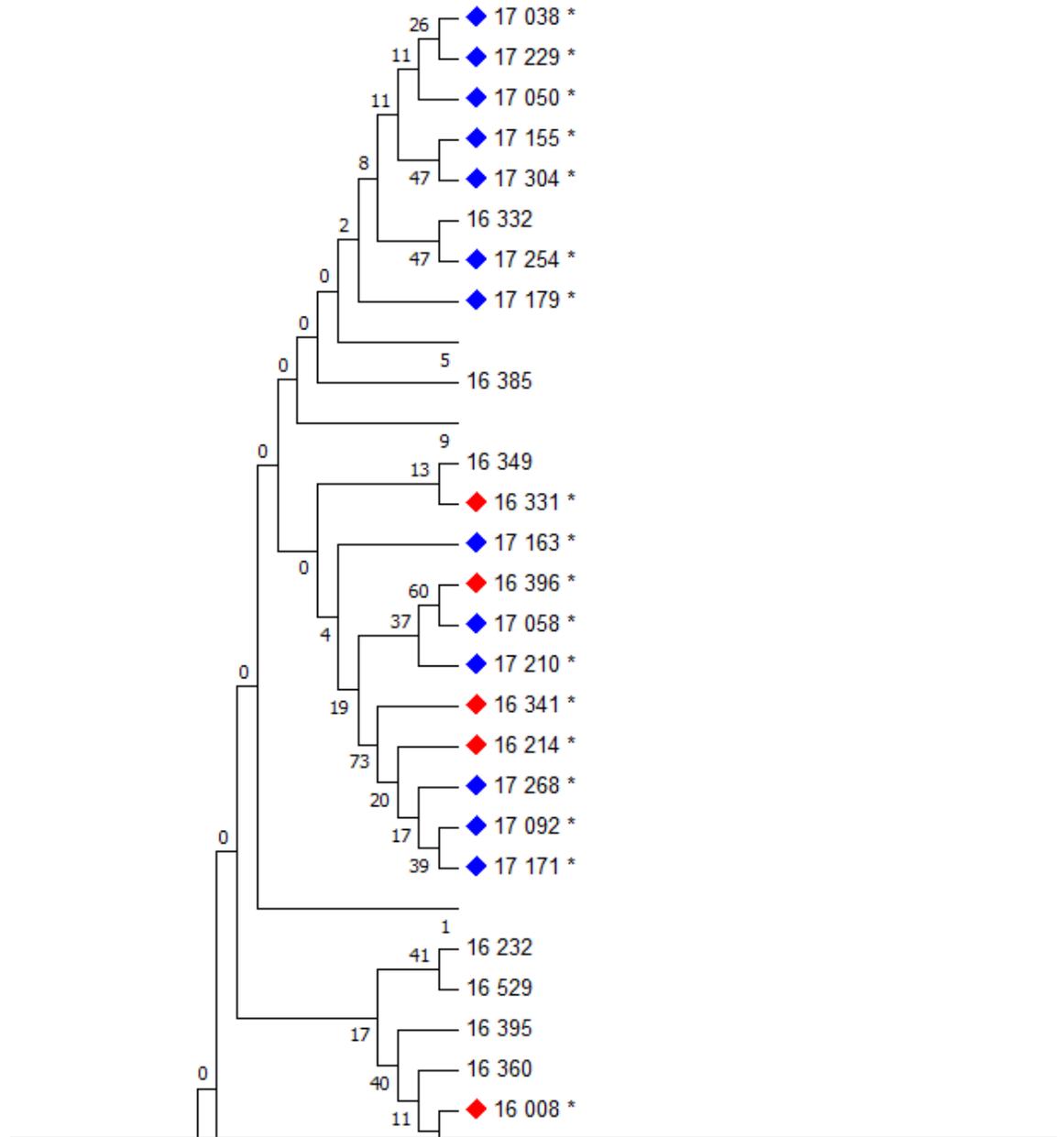
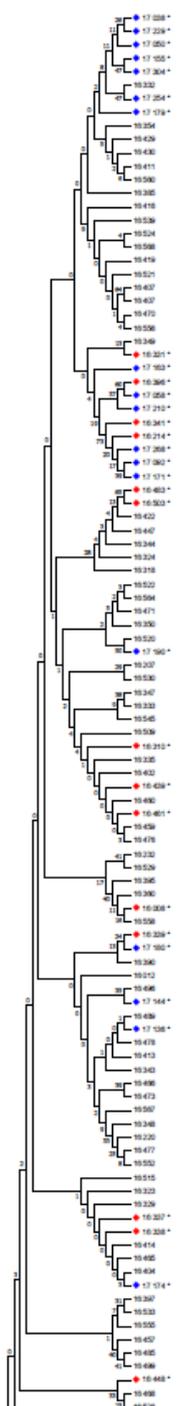
Ülkemizde Genel Durum

	Korten ve ark.	Sayan ve ark.	Kuskucu ve ark.		Sertöz ve ark.
n	273	1306	590		483
Dönem	2011	2010-2015	2004-2010	2011-2015	2008-2016
NRTI	6,90%	8,10%	5,92%	5,23%	3,0%
NNRTI	0,00%	3,30%	3,55%	4,04%	10,3% (5,0% E138A)
PI	1,70%	2,30%	0,60%	1,60%	1,8 %
Any	8,60%	10,10%	10,00%		15,0%

E138 Mutasyonları

Yıl	n	E138AG	%
2009	42	1	2.38%
2010	68	3	4.41%
2011+2012	43	3	6.98%
2013	62	3	4.84%
2014	172	15	8.72%
2015	486	47	9.67%
2016	382	51	13.35%
2017	264	24	9.09%







Stanford University HIV DRUG RESISTANCE DATABASE

A curated public database to represent, store and analyze HIV drug resistance data.

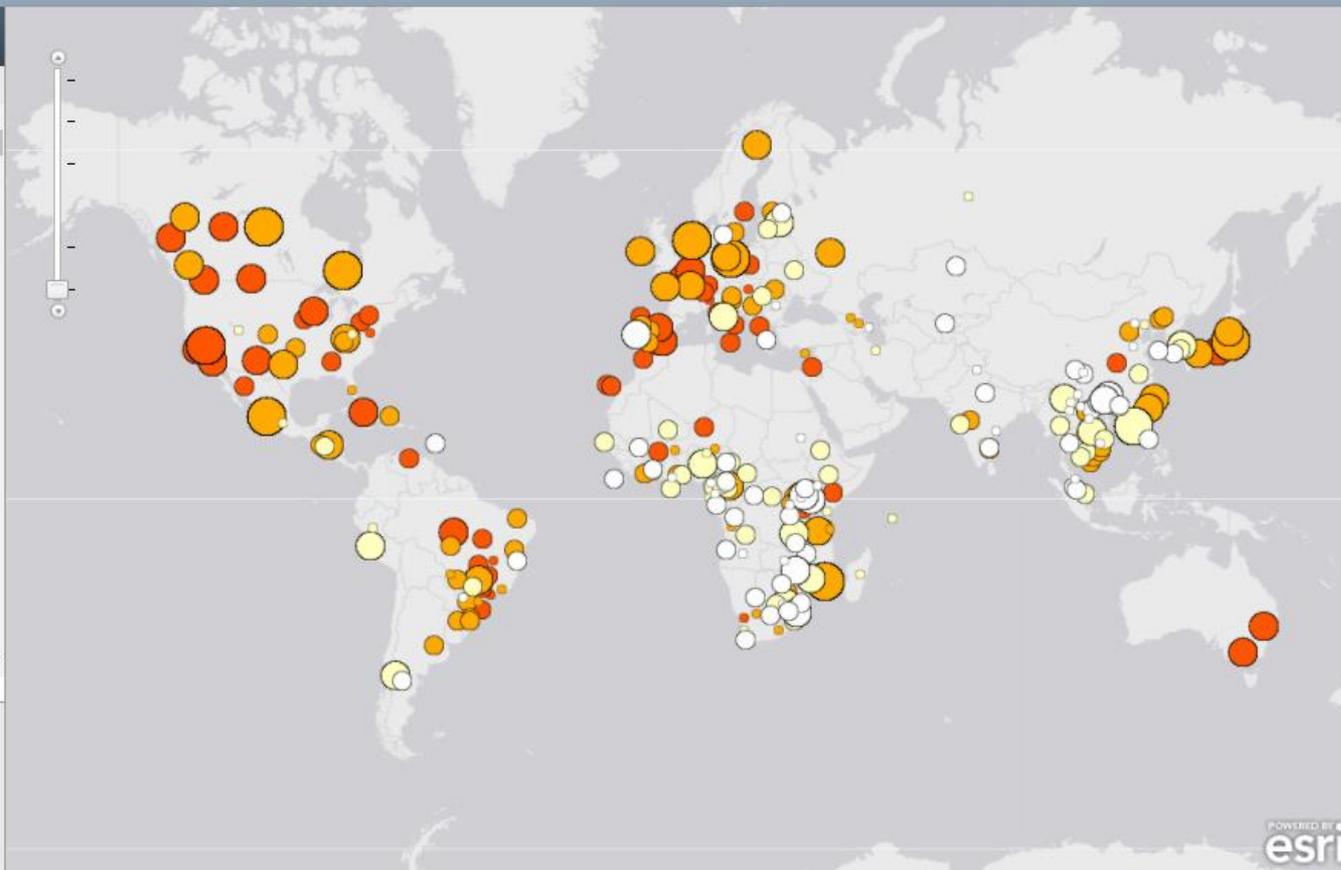
HOME GENOTYPE-RX GENOTYPE-PHENO GENOTYPE-CLINICAL HIVdb PROGRAM ABOUT HIVdb

HIV-1 Drug Resistance in ARV-naive Populations

Compendium of published virus sequences from 50,869 persons, 287 studies according to region, year and subtype

Publications

Continent	Country	Publication	Resistance (%)	n
Africa	ANGOLA	Yang10	0	39
Africa	ANGOLA	Bartolo14	2.1	140
Africa	ANGOLA	Bartolo09	4.1	121
Africa	ANGOLA	Castelbranco10	5.7	35
Africa	BENIN	Chamberland12	3.9	127
Africa	BOTSWANA	Bussmann05	0	71
Africa	BOTSWANA	Bussmann11	1.3	152
Africa	BURKINA FASO	Somda12	6.2	48
Africa	BURKINA FASO	Tebit09	12.5	104
Africa	BURKINA FASO CAME	Vergne08	3.1	195
Africa	BURKINA FASO COTE D'IVOIRE SE	Ayoubu00_Africa	0.7	147
Africa	BURUNDI	Vidal07	1	105
Africa	CAMEROON	Carr05_Africa	0	91
Africa	CAMEROON	Njai06	0	27
Africa	CAMEROON	Vessiere06	2.1	95
Africa	CAMEROON	Ndemb08	2.7	74
Africa	CAMEROON	Youngpairo12	3.5	57
Africa	CAMEROON	Billong13	3.6	139
Africa	CAMEROON	Soares10	4.1	49
Africa	CAMEROON	Aghokeng11	7.8	206
Africa	CAMEROON			



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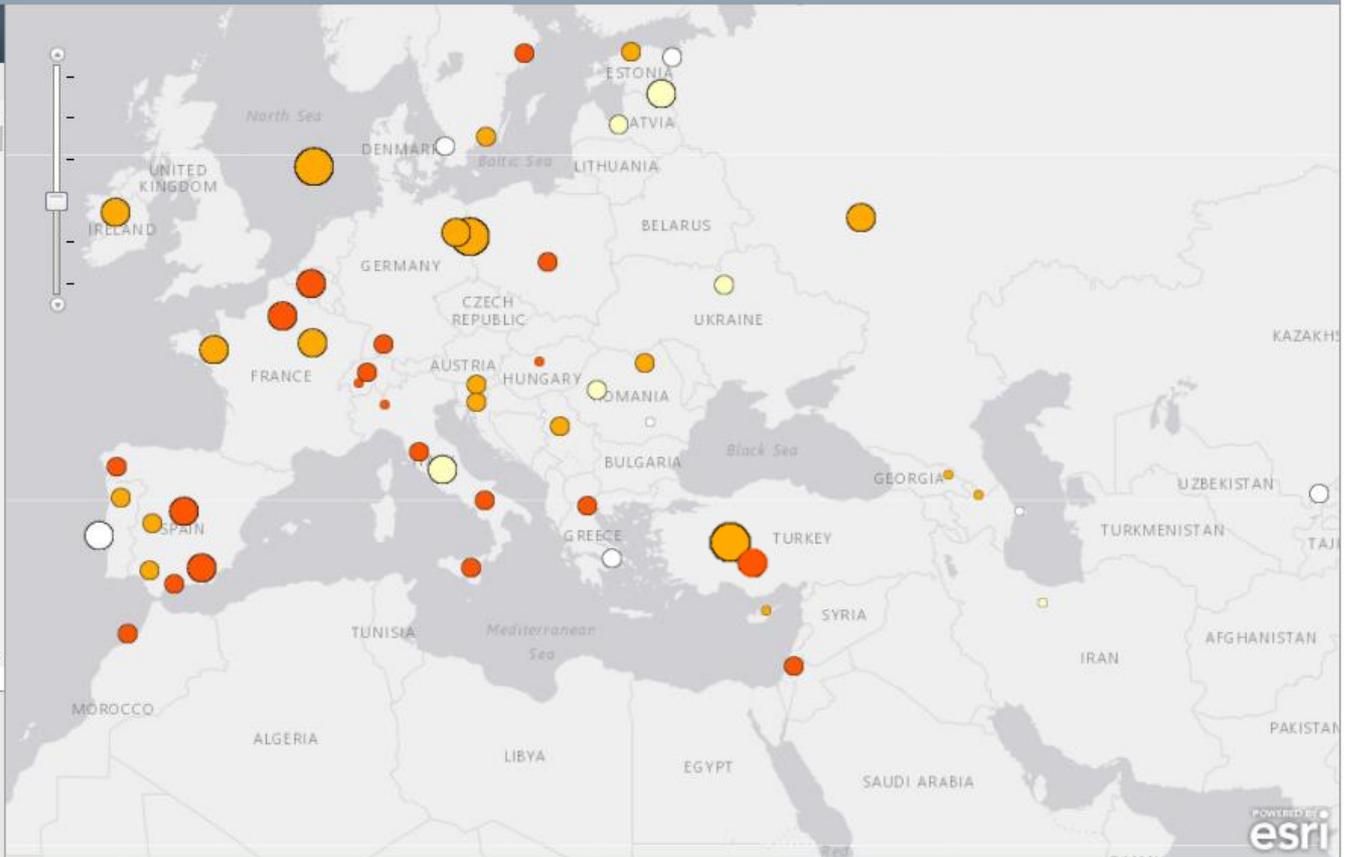
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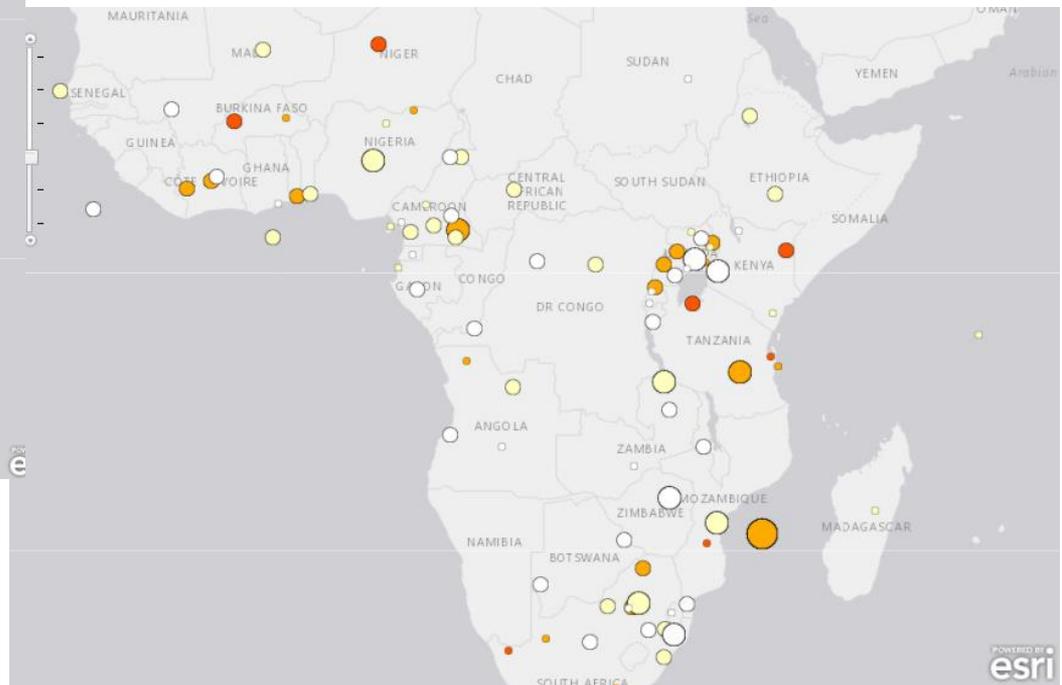
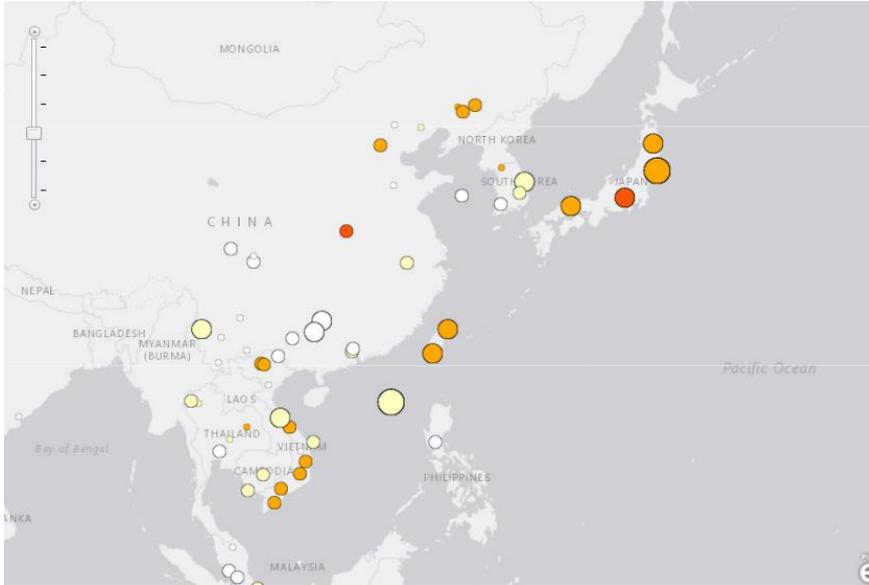
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Africa	CAMEROON	Carr05_Africa	0	91
Africa	CAMEROON	Njai08	0	27
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Africa	CAMEROON	Ndembio8	2.7	74
Africa	CAMEROON	Youngpair012	3.5	57
Africa	CAMEROON	Billong13	3.8	139
Africa	CAMEROON	Soares10	4.1	49
Africa	CAMEROON	Aghokeng11	7.8	208
Africa	CAMEROON			

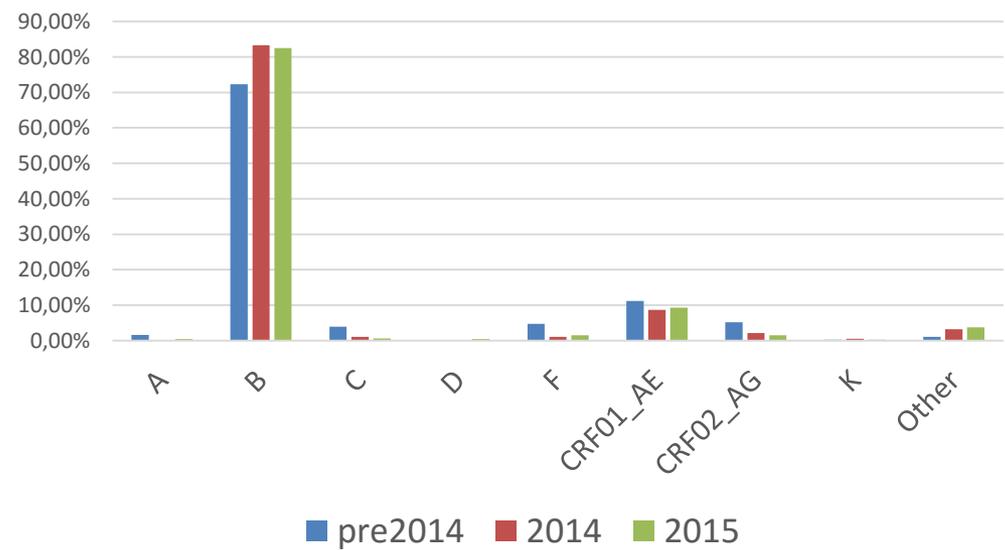
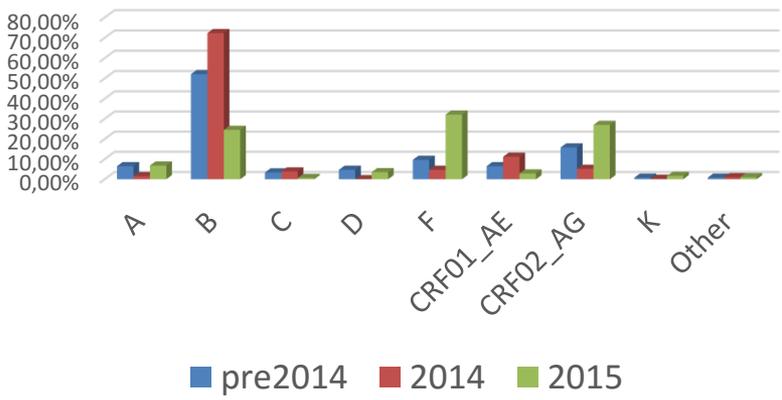


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Protease





*Ilaç Direnci:
Korkalım mı?*

Tesekkürler...