

HIV Transmitted Drug Resistance In Ireland 2023





Technical Notes – Explanation of Terms

HIV Drug Resistance (HIVDR): is caused by one or more changes (mutations) in the genetic structure of HIV that affect the ability of a specific drug or combination of drugs to block replication of HIV

Transmitted Drug Resistance (TDR): occurs when individuals are infected with HIV that has drug resistance mutations. TDR is detected in people living with HIV with no history of antiretroviral drug exposure (ART –Naïve)

ART-Naïve: applies to people with no history of anti retroviral drug exposure

Genotypic Antiretroviral Resistance Testing (GART) analyses HIV genetic material to identify mutations that cause resistance to antiretroviral drugs

Surveillance Drug Resistance Mutations(SDRM): as defined by hivdb.stanford.edu

Antiretroviral Treatment (ART): HIV antiretroviral drugs are categorised by drug class

- Nucleoside-analogue reverse transcriptase inhibitors (NRTIs), block reverse transcriptase, an enzyme used by HIV to replicate
 itself
- Non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs) also block reverse transcriptase. NNRTIs have played an important role in the management of HIV-1 infections in resource-limited countries
- Protease inhibitors (PI) prevent HIV replication by selectively binding to viral proteases and inhibiting maturation of the virus
- Integrase strand transfer inhibitors (InSTIs), block HIV integrase, used by HIV to insert its viral RNA (in cDNA form) into the DNA of the host CD4 cell. InSTI's are playing an increasing role in management of HIV-1 infections in low- and middle-income countries.



Public Health Implications

- Global and national policy decisions on antiretroviral therapy and HIV service delivery need to be informed by reliable national data on HIV drug resistance (HIVDR) prevalence and trends.
- As therapies become more widely available, the potential for HIVDR and HIVTDR increases
- WHO recommends population-based surveillance of TDR to monitor its prevalence and distribution,
 which can inform public health policy and treatment guidelines
- Increasing levels of HIVTDR may limit first line treatment options, lead to therapy failures or result in new infections in the context of preexposure or postexposure prophylaxis (PrEP and PEP)
- In Ireland, it is welcome news that trends in HIVTDR have remained stable since 2017
- HPSC will continue to report trends in HIVTDR periodically





Key Points 2023

- Results of this analysis should be interpreted with caution as data completeness varies and small sample size for subgroups make trend analysis difficult.
- In Ireland, HIVTDR data from 2023 shows rates remain steady (6.8%; CI 3.7-12.2) compared to data from 2017-2019 and 2021.
- There were no PI and InSTI related TDR and all cases of TDR were to a single drug class only.
- TDR to NRTI drugs in 2023 (0.7%; CI 0.1- 3.8) was lower than the rate reported in 2021. TDR remains steady for NNRTI drugs in 2023 (6.3%; CI 3.3-11.5), with no significant difference from data analysed in 2017- 2019 and 2021
- The most common subtype among TDR cases was subtype B (n=5), followed by subtype C (n=3)
- Despite annual fluctuations, aggregated data from 2017-2019, 2021 and 2023 show no significant difference in HIVTDR prevalence by sex/gender, age group, region of origin, probable route of transmission or subtype



 HIVTDR rates in Ireland are comparable to those in international studies although comparisons should be made cautiously as study criteria vary



Technical Notes – Methods

- In Ireland, HIV has been notifiable since 2011. All cases that comply with the <u>case definition</u> are reported via the national Computerised Infectious Disease Reporting (CIDR) system
- Since 2017, case-based HIV epidemiological data from CIDR are linked to HIVDR data provided by the National Virus Reference Laboratory (NVRL), to produce national TDR prevalence rates
- Since 2019 HIVTDR reports are produced biennially.
- Criteria for inclusion in this surveillance report: A person aged ≥18 years, living with HIV-1 who has been tested prior to commencing their first ART regimen in Ireland for susceptibility to any of the available antiretroviral (ARV) drugs in the four main drug classes: NRTIs, NNRTIs, PIs, and InSTIs
- Persons are identified as having TDR using HIVDR data from NVRL in combination with information on prior exposure to ART from CIDR*
- Testing conducted in NVRL was by Sanger sequencing and analysed using <u>Stanford University HIV Drug</u> <u>Resistance Database</u>
- 2023 epidemiological data used in this report were extracted from CIDR on 18/08/2025 and were correct at that time. Further information on HIV in Ireland in 2023 can be found here
- The Surveillance HIV-1 Drug Resistance Mutations (SDRM) list used in this report can be found at <u>hivdb.stanford.edu</u> This table includes World Health Organization (WHO) SDRM 2009 list, and the integrase strand transfer inhibitor (INSTI) SDRM 2019 list
- Ninety-five percent confidence intervals (CI) were computed using the Wilson score interval for binomial proportions

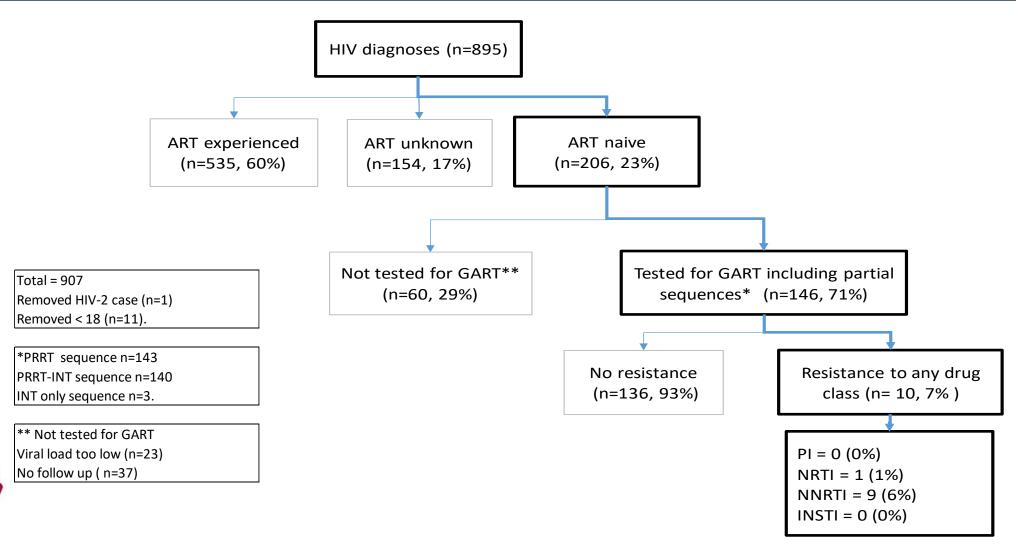
^{*} CIDR variables: "When did patient start ART" and "Date ART started"





Transmitted HIV drug resistance (TDR) in Ireland 2023



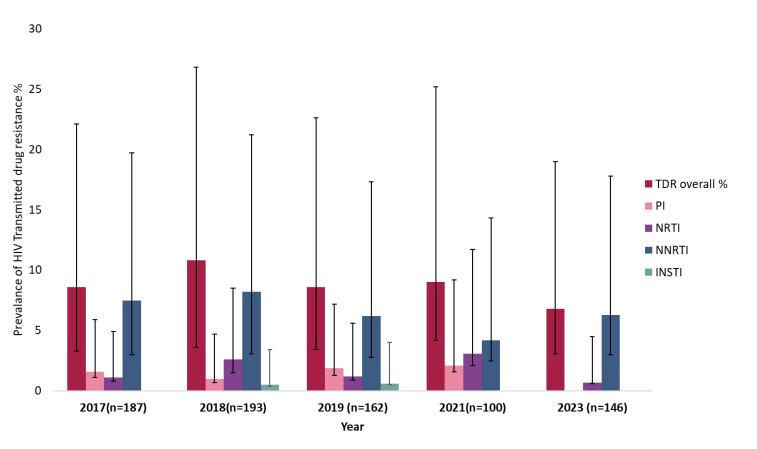






Percentage TDR prevalence in ART naïve individuals tested for GART 2017-2019, 2021 & 2023





1	1	Prevalence of		1
		TDR %	Lower 95% CI	Higher 95% CI
	2017	8.6	5.3	13.5
	2018	10.8	7.2	16
	2019	8.6	5.2	14
	2021	9	4.8	16.2
Total	2023	6.8	3.7	12.2
	2017	1.6	0.5	4.3
	2018	1	0.3	3.7
	2019	1.9	0.6	5.3
	2021	2.1	0.5	7.1
PI	2023	N/A	N/A	N/A
	2017	1.1	0.3	3.8
	2018	2.6	1.1	5.9
	2019	1.2	0.3	4.4
	2021	3.1	1	8.6
NRTI	2023	0.7	0.12	3.8
	2017	7.5	4.5	12.2
	2018	8.2	5.1	13
	2019	6.2	3.4	11.1
	2021	4.2	1.7	10.1
NNRTI	2023	6.3	3.3	11.5
	2017	N/A	N/A	N/A
	2018	0.5	0.1	2.9
	2019	0.6	0.1	3.4
	2021	N/A	N/A	N/A
INSTI	2023	N/A	N/A	N/A



Data from 2020 and 2022 were not analysed.



TDR prevalence in ART naïve individuals tested for GART 2023 by gender and age group



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	95	% CI
		N	N	%	%	%
Total		146	10	6.8	3.7	12.2
Gender	Male	109	7	6.4	3.1	12.7
	Female	37	3	8.1	2.7	21.3
Age group (years)	18-24	11	1	9.1	1.6	37.7
	25-34	52	3	5.8	1.9	15.6
	35-44	45	5	11.1	4.8	23.5
	45+	38	1	2.6	0.5	13.5



Data presented by the gender male includes cis male and trans male and data presented by the gender female includes cis female and trans female.

TDR prevalence in ART naïve individuals tested for GART 2023 by region of birth



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	95	% CI
		N	N	%	%	%
Total		146	10	6.8	3.7	12.2
Region of origin	Ireland	35	2	5.7	1.6	18.6
	Sub-Saharan Africa	41	3	7.3	2.5	19.4
	Latin America & Caribbean	25	2	8.0	2.2	24.9
	Europe	30	2	6.7	1.8	21.3
	Other /Unknown	15	1	6.7	1.2	29.8





TDR prevalence in ART naïve individuals tested for GART 2023 by probable route of transmission



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	959	% CI
		N	N	%	%	%
Total		146	10	6.8	3.7	12.2
	gbMSM*	57	4	7.0	2.7	16.7
Drobable route of	Hetero Male	41	2	4.9	1.3	16.1
Probable route o transmission	Hetero Female	35	2	5.7	1.6	18.6
	PWID**	3	1	33.3	6.1	79.2
	Other /Unknown	10	1	10.0	1.8	40.4



^{*}gay bisexual and other men who have sex with men (gbMSM)

^{**} People who inject drugs (PWID)



TDR prevalence in ART naïve individuals tested for GART 2023 by HIV subtype



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	959	% CI
		N	N	%	%	%
Total		146	10	6.8	3.7	12.2
	A1	4	1	25.0	4.5	70.0
	A6	19	0	N/A		
	В	42	5	11.9	5.2	25.0
	С	53	3	5.7	1.9	15.4
Cubtupa	D	2	0	N/A		
Subtype	F	2	0	N/A		
	G	2	0	N/A		
	CRF01_AE	10	0	N/A		
	CRF02_AG	8	1	12.5	2.2	47.1
	Other*	4	0	N/A		



*Other includes CRF24 BG (n=1), Subtype B+F (n=1) and Subtype B+G(n=2)



TDR by demographic characteristics subtype and drug class in ART naïve individuals 2023



n=10		NRTI	NNRTI	Total
		N	N	N
Gender	Male	1	6	7
	Female	0	3	3
Age group (years)	18-24	1	0	1
	25-34	0	3	3
	35-44	0	5	5
	45+	0	1	1
Region of origin	Ireland	0	2	2
	Sub-Saharan Africa	0	3	3
	Latin America & Caribbean	0	2	2
	Europe	0	2	2
	Other /Unknown	1	0	1
	gbMSM	1	3	4
Drobable route of	Hetero Male	0	2	2
Probable route of transmission	Hetero Female	0	2	2
11 01151111551011	PWID	0	1	1
	Other /Unknown	0	1	1
	A1	0	1	1
Subtype	В	1	4	5
	С	0	3	3
	CRF02_AG	0	1	1





Surveillance drug resistance mutations(SDRM) in ART naïve individuals Ireland 2023



	SDRM	N
NRTI Mutations	M41L	1
	T215E	1
NNRTI Mutations	K103N	7
	K103S	1
	G190A	1
	P225H	2

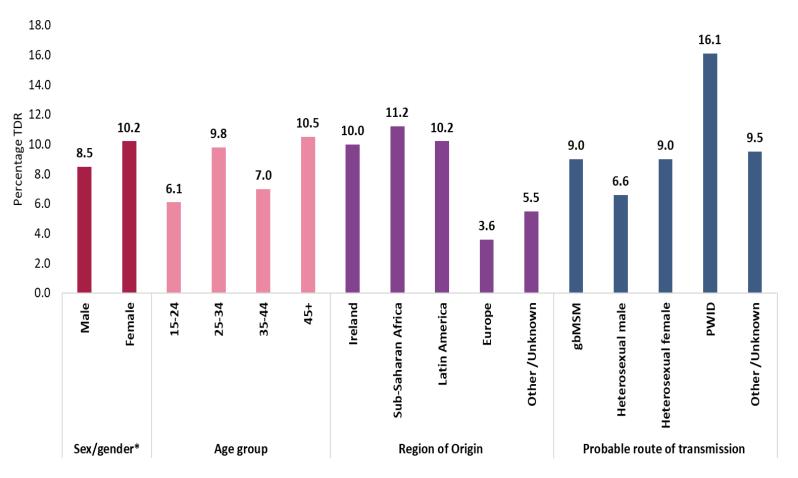


More than one SDRM may be present in the HIV amplicons analysed from ART naïve individuals



TDR Prevalence in ART naïve individuals by demographic characteristic –aggregated data from 2017-2019, 2021 and 2023





		CL95	CL95
	TDR %	lower	higher
Male	8.5	6.6	11.0
Female	10.2	6.4	15.7
15-24	6.1	2.4	14.6
25-34	9.8	6.9	13.5
35-44	7.0	4.3	11.2
45+	10.5	6.9	15.6
Ireland	10.0	7.0	14.0
Sub-Saharan			
Africa	11.2	7.4	16.7
Latin America	10.2	6.1	16.7
Europe	3.6	1.5	8.1
Other			
/Unknown	5.5	1.9	14.8
gbMSM	9.0	6.6	12.2
Heterosexual			
male	6.6	3.6	11.7
Heterosexual			
female	9.0	5.4	14.6
PWID	16.1	9.1	32.6
Other			
/Unknown	9.5	3.8	22.1

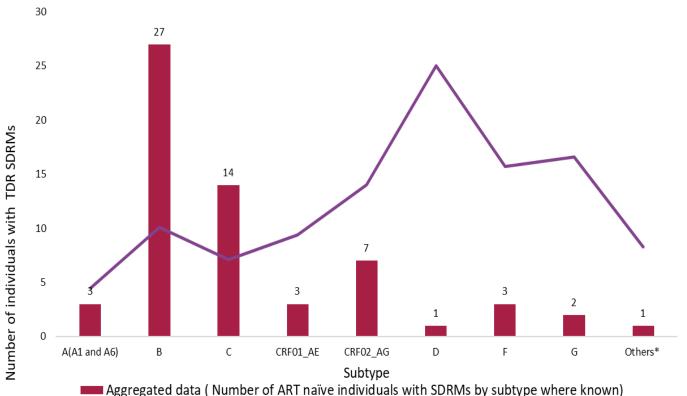


^{*}Data from 2017-2019 were analysed by sex at birth and data from 2021 and 2023 were analysed by gender which means male includes cis male and trans male and data presented by the gender female includes cis female and trans female.

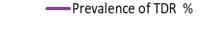


TDR Prevalence in ART naïve individuals by subtype – aggregated data from 2017-2019 and 2023





	Prevalence of TDR		
Subtype	%	CI95 Lower	CI95 higher
A(A1 and A6)	4.5	1.5	12.5
В	10.1	7	14.3
С	7.1	4.3	11.7
CRF01_AE	9.4	3.2	24.2
CRF02_AG	14	6.9	29.2
D	25	4.5	69.9
F	15.7	5.5	37.6
G	16.6	4.7	44.8
Others*	8.3	1.4	35.3



^{*}Others: Subtypes include subtype J, CRF06 cpx, CRF24 BG, CRF12 BF, Subtype B+F, Subtype B+G.



In 2021, due to the impact of the COVID-19 pandemic NVRL sent samples to Colindale UK for GART. Details of HIV subtype for 2021 data were not available for this analysis.



TDR Prevalence - International

- Direct comparison between international studies is not always possible as study criteria vary.
- A study of TDR and subtype patterns of viruses from reported new HIV diagnoses in <u>Germany, 2017–2020</u> calculates TDR at 4.3% (95% CI, 3.7- 4.8) for NRTIs, 9.2% (95% CI, 8.4-10.1) for NNRTIs, 3.3% (95% CI, 2.8- 3.8) for PIs and 1.4% (95% CI, 0.9-1.8) for InSTIs. All rates are higher than those reported in 2023 in Ireland
- In 2019 <u>ECDC</u> reported on a pilot study (2017) which estimated TDR from case-based data submitted by six European countries to be 14.5% and TDR was estimated at 10.8% from four countries that supplied aggregate data. The study used the Stanford HIVdb to determine drug resistance and not the surveillance drug resistance mutation (SDRM) list 2009
- In November 2021 WHO published the HIV Drug Resistance Report which described the prevalence of pretreatment HIV drug resistance among adults, including those who were who were ART naïve and initiated ART between 2014—2020 in low- and middle-income countries. Overall, the prevalence of HIV drug resistance in those with out previous ART drug exposure was 7.2% (95% CI 4.3-10.2) for NNRTIs is higher than the 2023 rate in Ireland (6.3%; CI 3.3-11.5). The overall prevalence of HIV drug resistance in those without previous ART drug exposure for NRTIs was 2.8% (95% CI 1.4-4.3), also higher than the 2023 rate in Ireland (0.7%; CI 0.1-3.8)



WHO's brief 2024 HIV drug resistance report summarizes recent information on HIV drug resistance in InSTIs in lowand middle-income countries. No HIVTDR to InSTIs was reported in 2023 in Ireland

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