



# HIV Transmitted Drug Resistance In Ireland 2021 - February 2024





## Key Points

- HIV transmitted drug resistance (HIVTDR) is a global problem.
- Access to effective antiretroviral treatment is critical for all individuals living with HIV and is an important tool in HIV prevention.
- Periodic HIVTDR surveillance is useful at country level and globally to inform treatment guidelines and policies.
- In Ireland HIVTDR data from 2021 shows rates remain steady at 9.0%, similar to HIVTDR values in Ireland between 2017-2019.
- HIVTDR by drug class also remains steady in 2021 and all cases of TDR were to a single drug class only.
- Aggregated data from 2017-2021 show no significant difference in HIVTDR prevalence by sex/gender, age group, region of origin or probable route of transmission.
- HIVTDR rates in Ireland are comparable to those calculated in international studies although study criteria vary.



# Acknowledgements

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- Microbiology laboratories
- Departments of Public Health
- Sexual Health and Crisis Pregnancy Programme (SHCPP)
- Consultants in Infectious Disease/Genitourinary Medicine
- GPs
- HIV clinical nurse specialists
- Health Advisors
- All other clinical staff involved.

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# Background

HIV drug resistance (HIVDR) is the ability of HIV to replicate and evolve in the presence of antiretroviral drugs. Transmitted drug resistance (TDR) is detected among antiretroviral drug (ART)-naïve people with no history of antiretroviral drug exposure. TDR occurs when previously uninfected individuals are infected with virus that has drug resistance mutations.

HIV TDR surveillance is important as WHO reports that all HIV antiretroviral drugs are at risk of becoming ineffective, as therapies become more widely available the potential for HIVDR, and HIVTDR increases.

Consequences include:

- Treatment failure
- Transmission of HIVDR
- Implications for first line treatment options
- Implications for national treatment guidelines



# HIV Drug Resistance In Ireland

- In Ireland, HIV has been notifiable since 2011 under the Infectious Disease Regulations as per the [case definition](#) all cases are reported via the Computerised Infectious Disease Reporting (CIDR) system
- Since 2017, case-based HIV epidemiological data from CIDR are linked to HIVDR data provided by the NVRL, to produce national TDR prevalence rates
- No TDR data were available for 2020 due to the impact of the COVID-19 pandemic
- HIV notifications in 2021 have been impacted by the COVID-19 pandemic due to reduced sexual health and GP services, reduced testing opportunities and reduced levels of inward migration



# Technical Notes – Explanation of Terms

**GART - genotypic antiretroviral resistance testing (GART)**

**HIV antiretroviral drugs are categorised by drug class**

- **NRTI Nucleoside-analogue reverse transcriptase inhibitors (NRTIs)**, block reverse transcriptase, an enzyme used by HIV to replicate itself
- **NNRTI 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
- **PI Protease inhibitors (PI)** prevent HIV replication by selectively binding to viral proteases and inhibiting maturation of the virus
- **InSTI 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





# Technical Notes – Methods

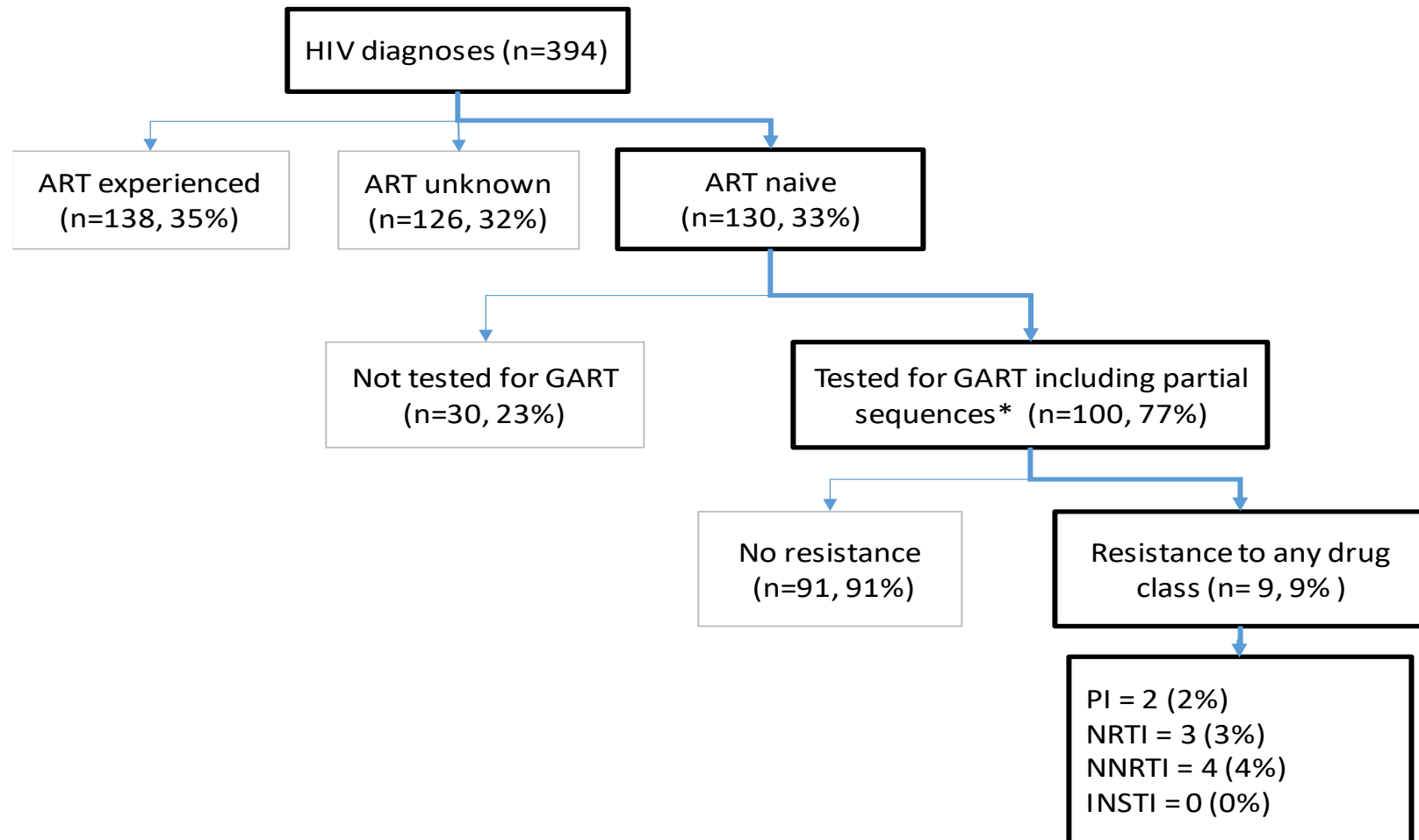
- **Criteria for inclusion in this surveillance report:** A person aged  $\geq 18$  years, living with HIV-1 who has been tested prior to commencing their first ART regimen in Ireland for susceptibility to any of the available antiretroviral (ARV) drugs in the four main drug classes: NRTIs, NNRTIs, PIs, and InSTIs
- Persons are identified as having TDR using HIVDR data from NVRL in combination with information on prior exposure to ART from CIDR\*
- In 2021 due to the impact of the COVID-19 pandemic NVRL was obliged to send some samples requiring GART to Colindale UK for analysis. If testing was conducted in NVRL sequences were generated using the sanger method and analysed using [Stanford University HIV Drug Resistance Database](#)
- 2021 epidemiological data used in this report were extracted from CIDR on 03/11/2023 and were correct at that time
- The surveillance HIV-1 Drug Resistance Mutations (SDRM) list used in this report can be found at [hivdb.stanford.edu](http://hivdb.stanford.edu) 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 2021



## All HIV diagnoses 2021

Total = 399  
-Removed HIV-2 case (1)  
-Removed < 18y (4)

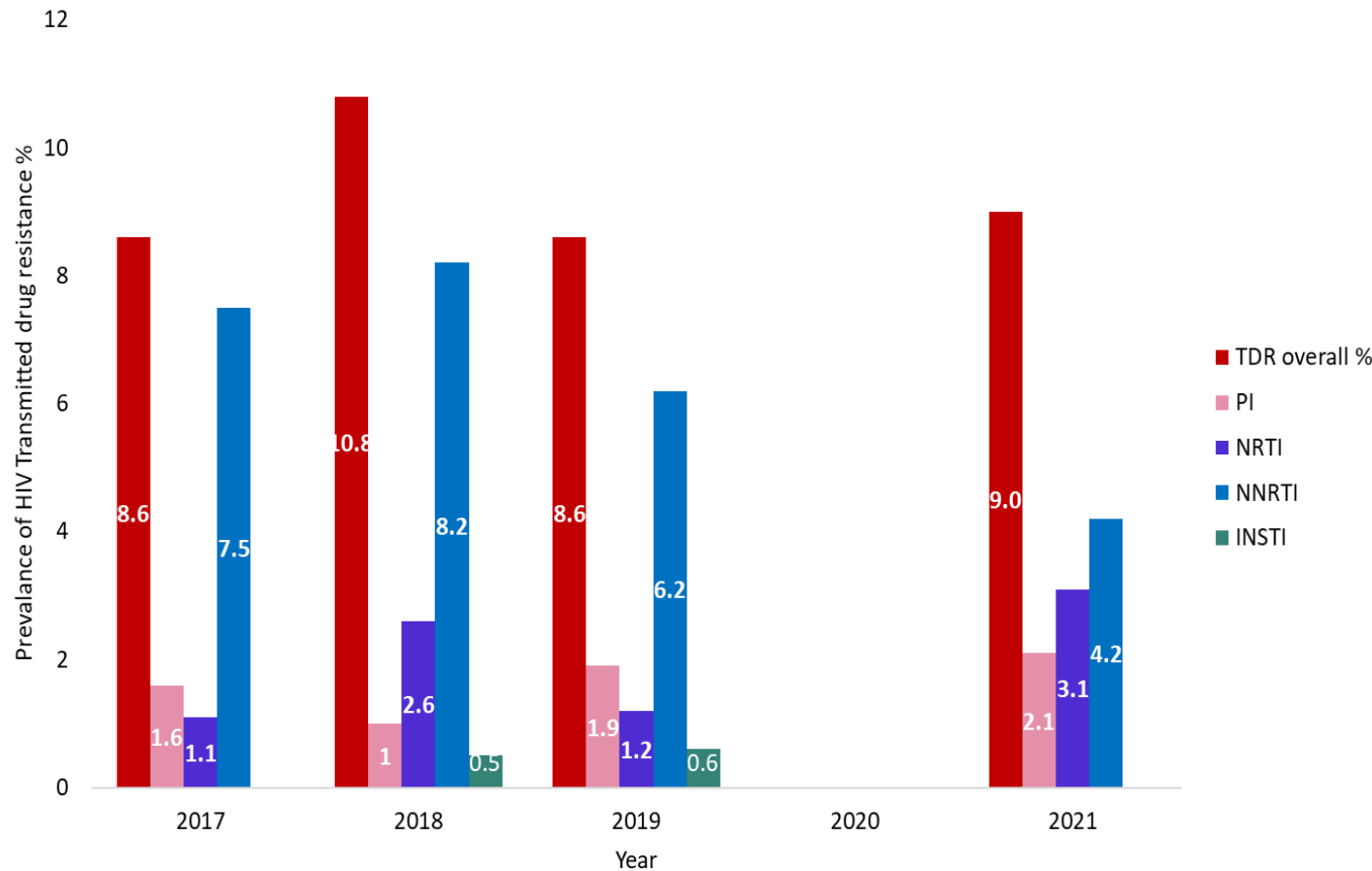
\*PRRT sequence n=96  
PRRT-INT sequence n=93  
INT only sequence n=4.







# Percentage TDR prevalence in ART naïve individuals tested for GART 2017-2021\*



		Prevalence of TDR	Lower 95% CI	Higher 95% CI
Total	2017	8.6	5.3	13.5
	2018	10.8	7.2	16
	2019	8.6	5.2	14
	2020	n/a	n/a	n/a
	2021	9	4.8	16.2
PI	2017	1.6	0.5	4.3
	2018	1	0.3	3.7
	2019	1.9	0.6	5.3
	2020	n/a	n/a	n/a
	2021	2.1	0.5	7.1
NRTI	2017	1.1	0.3	3.8
	2018	2.6	1.1	5.9
	2019	1.2	0.3	4.4
	2020	n/a	n/a	n/a
	2021	3.1	1	8.6
NNRTI	2017	7.5	4.5	12.2
	2018	8.2	5.1	13
	2019	6.2	3.4	11.1
	2020	n/a	n/a	n/a
	2021	4.2	1.7	10.1
INSTI	2018	0.5	0.1	2.9
	2019	0.6	0.1	3.4



\*Data not available for 2020 due to COVID-19 pandemic and reduced GART testing



# TDR prevalence in ART naïve individuals tested for GART 2021 by gender and age group



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	95% CI	
		N	N	%	%	%
Total		100	9	9.0	4.8	16.2
Gender	Male	87	5	5.7	2.4	12.7
	Female	13	4	30.8	12.6	57.6
Age group (years)	18-24	6	0	0.0	0.0	39.0
	25-34	41	4	9.8	3.8	22.5
	35-44	21	0	0.0	0.0	15.4
	45+	32	5	15.6	6.8	31.7



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 2021 by region of birth



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	95% CI	
		N	N	%	%	%
Total		100	9	9.0	4.8	16.2
Region of origin	Ireland	50	6	12.0	5.6	23.8
	Sub-Saharan Africa	10	2	20.0	5.6	50.9
	Latin America	13	0	0.0	0.0	22.8
	Europe	19	1	5.3	0.9	24.6
	Other /Unknown	8	0	0.0	0.0	25.9





# TDR prevalence in ART naïve individuals tested for GART 2021 by probable route of transmission



		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	95% CI	
		N	N	%	%	%
Total		100	9	9.0	4.8	16.2
	gbMSM*	64	3	4.7	1.6	12.9
Probable route of transmission	Hetero Male	15	2	13.3	3.7	37.8
	Hetero Female	11	3	27.3	9.7	56.5
	PWID**	4	0	0.0	0.0	48.9
	Other /Unknown	6	1	16.7	3.0	56.3



\*gay bisexual and other men who have sex with men (gbMSM)

\*\* People who inject drugs (PWID)



# TDR by demographic characteristics and drug class in ART naïve individuals 2021



n=9		PI	NRTI	NNRTI	Total
		N	N	N	N
Gender	Male	1	2	2	5
	Female	1	1	2	4
Age group (years)	25-34	0	1	3	4
	45+	2	2	1	5
Region of origin	Ireland	2	3	1	6
	Sub-Saharan Africa	0	0	2	2
	Europe	0	0	1	1
Probable route of transmission	gbMSM	1	1	1	3
	Heterosexual	0	2	3	5
	Other /Unknown	1	0	0	1





# Surveillance drug resistance mutations in ART naïve individuals Ireland 2021

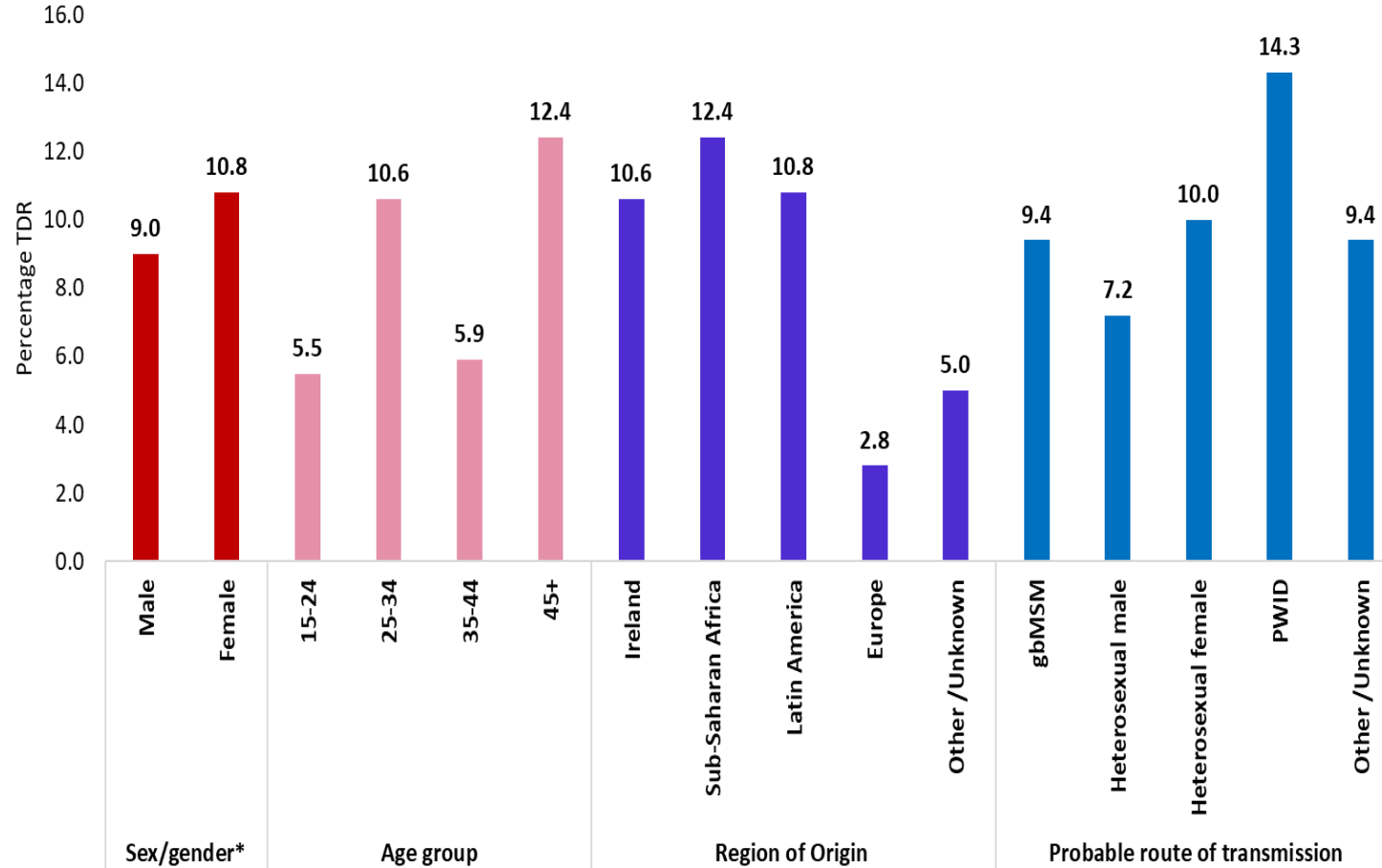


		N
PI Mutations	M46I	1
	D30N	1
NRTI Mutations	T69D	1
	T215E	2
NNRTI Mutations	K103N	9
	P225H	1





# TDR Prevalence in ART naïve individuals by demographic characteristic –aggregated data from 2017-2021



		TDR	CL95 lower	CL95 higher
Sex/gender*	Male	9.0	6.79	11.75
	Female	10.8	6.52	17.27
Age group	15-24	5.5	1.87	14.85
	25-34	10.6	7.41	14.85
	35-44	5.9	3.24	10.55
	45+	12.4	8.09	18.58
Region of Origin	Ireland	10.6	7.38	14.97
	Sub-Saharan Africa	12.4	7.89	18.97
	Latin America	10.8	6.13	18.29
	Europe	2.8	0.94	7.78
	Other /Unknown	5.0	1.38	16.5
Probable route of transmission	gbMSM	9.4	6.75	12.87
	Heterosexual male	7.2	3.69	13.58
	Heterosexual female	10.0	5.81	16.67
	PWID	14.3	5.69	31.49
	Other /Unknown	9.4	3.24	24.22



\*Data from 2017-2019 were analysed by sex at birth and 2021 data 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.

# Summary

- **Results of this analysis should be interpreted with caution as data completeness varies and small sample size for subgroups make trend analysis difficult.**
- The prevalence of TDR in Ireland in 2021 remains steady at 9.0%, this value is not statistically significantly different to TDR values for Ireland between 2017-2019.
- TDR by drug class also remains steady and fluctuations observed for PI , NRTI and NNRTI drug classes are not statistically significant, in 2021 there was no InSTI related TDR and all cases of TDR were to a single drug class only.
- Despite annual fluctuations, aggregated data from 2017-2021 show no significant difference in HIVTDR prevalence by sex/gender, age group, region of origin or probable route of transmission.



# HE TDR Prevalence - International

- **Direct comparison between international studies is not always possible as study criteria vary.**
- In November 2021 [WHO](#) published the latest HIV Drug Resistance Report which described the prevalence of pretreatment HIV drug resistance among adults initiating ART between 2014–2020 in low and middle income countries, who were ART naive. Overall NNRTI TDR rate was 7.2% (95% CL 4.3-10.2) which is higher than the 2021 rate in Ireland (4.2%). The prevalence of NRTI TDR was 2.8% (95% CL 1.4- 4.3) and is similar to the 2021 NRTI TDR rate of 3.1% in Ireland. PI TDR cannot be compared as WHO reported TDR for a restricted number of PI drugs:
- In 2019 [ECDC](#) 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.
- A study published in [2020](#) estimates TDR from 2902 ART- naïve individuals from 35 countries to be 4.9% for NNRTI, 3.2% NRTI, 2.4% PI and 0.1% INSTI at the sanger sequencing detection threshold (20%). These values are similar to 2021 TDR rates in Ireland.



## Conclusion

- Periodic monitoring of HIVTDR in newly diagnosed HIV patients at initiation of antiretroviral treatment is useful at country level and globally to inform treatment guidelines and policies.
- Timely initiation of effective antiretroviral treatment is critical for individuals, and successful treatment prevents onward transmission of HIV to sexual partners.
- An **undetectable** HIV viral load **equals** **untransmissible** HIV infection (**U=U**), this is an important public health message which along with other HIV prevention measures has the power to end HIV.