HIV Drug Resistance in Ireland, 2018

Version 1.1
September 2021

Key Points

- Of 523 HIV diagnoses in 2018, history of exposure to antiretroviral therapy (ART) was available for 82% (n=430); 43% were ART-naïve, 39% were ART-experienced and 18% were ART-unknown.
- HIV drug resistance testing could be carried out for 51% (n=266) of people diagnosed, and could not be carried out for 49% (n=257) mostly due to low viral loads indicative of viral suppression due to already being on effective ART.
- Of those who were ART-naïve, 86% (n=194) could be tested for HIV drug resistance.

Transmitted HIV drug resistance (TDR):

Of those who were ART-naïve and were tested for HIV drug resistance:

- Twenty individuals had surveillance drug resistance mutations (SDRMs), categorised using the World Health Organization (WHO) SDRM 2009 list, and the integrase strand transfer inhibitor (INSTI) SDRM 2019 list.
- Prevalence of TDR was 11% (95% CI 7.2% -16.0%), which was not significantly higher than the prevalence in 2017 (8.6%; 95% CI 5.3% - 13.5%).
- By drug class, prevalence of TDR was 8% for non-nucleoside reverse transcriptase inhibitors (NNRTIs), 3% for nucleoside-analogue reverse transcriptase inhibitors (NRTIs), 1% for protease inhibitors (PIs), and 0.5% for INSTIs.
- By region of origin, prevalence of TDR was 14% among people born in sub-Saharan Africa, 14% among people born in Latin America, and 9% among people born in Ireland.
- By probable route of transmission, prevalence of TDR was 12% among heterosexual males, 9% among heterosexual females, and 11% among men who have sex with men (MSM).

TDR among people recently infected:

- Among people likely recently infected (within four months prior to testing) where known, prevalence of TDR was 8% (95% CI 2.7%-20.3%).

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Explanation of terms

HIV drug resistance category

The World Health Organization (WHO) commonly classifies HIV drug resistance into three main categories (1):

ADR	Acquired drug resistance (ADR) develops because of viral replication in the presence of antiretroviral drugs.
TDR	Transmitted drug resistance (TDR) is detected among antiretroviral drug-naïve people with no history of antiretroviral drug exposure. TDR occurs when previously uninfected individuals are infected with virus that has drug resistance mutations.
PDR	Pretreatment HIV drug resistance (PDR) refers to resistance that is detected among people initiating first-line treatment for the first time, or among people reinitiating first-line treatment following a previous exposure. Examples of previous exposure include antiretroviral drugs for preventing mother-to-child transmission of HIV, pre-exposure prophylaxis (PrEP), and first-line antiretroviral therapy that was followed by a period of treatment interruption. PDR can be either transmitted or acquired.

HIV drug class and current treatment guidelines

HIV antiretroviral drugs are categorised by drug class based on how they interfere with the HIV life cycle. The four main drug classes are as follows:

NRTI	Nucleoside-analogue reverse transcriptase inhibitors (NRTIs) were the first antiretroviral class for HIV treatment. They work by blocking reverse transcriptase, an enzyme that HIV needs to replicate itself. Examples of NRTIs include emtricitabine and tenofovir, both of which are used in the formulation of HIV PrEP.
NNRTI	Non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs) also prevent HIV replication by blocking reverse transcriptase. NNRTIs have played an important role in the management of HIV-1 infections in resource-limited countries.
PI	Protease inhibitors (PIs) prevent HIV replication by selectively binding to viral proteases and inhibiting maturation of the virus.
INSTI	Integrase strand transfer inhibitors (INSTIs) are the newest antiretroviral class in HIV treatment. They work by blocking HIV integrase, which is used by HIV to insert its viral RNA (in cDNA form) into the DNA of the host CD4 cell.

In Ireland, guidelines from the British HIV Association (BHIVA), the European AIDS Clinical Society (EACS), the US Department of Health and Human Services (DHHS), and the WHO are used to make decisions regarding first line therapy (2). Triple-drug therapy, consisting of two

NRTIs plus a third agent from one of the other three drug classes (the choice of which depends on a number of factors including risk of poor adherence), is recommended for antiretroviral treatment-naïve people living with HIV. The WHO recommend the use of an unboosted INSTI with a high genetic barrier (e.g. dolutegravir) as a preferred third agent (3).

Background

HIV drug resistance (HIVDR) is the ability of HIV to replicate and evolve in the presence of antiretroviral drugs (1). The potential for HIVDR increases as therapies are used more widely; the WHO reports that currently all HIV antiretroviral drugs are at risk of becoming ineffective. Consequences include treatment failure, implications for first line treatment options and national treatment guidelines, and onward transmission of HIVDR (4).

HIVDR can be either acquired (ADR) or transmitted (TDR). Population surveillance of TDR is recommended to preserve treatment options and to control future HIV epidemics (4).

HIV became a notifiable disease in Ireland under the Infectious Disease Regulations in 2011. Since 2012, all diagnoses of HIV are reported using the national Computerised Infectious Disease Reporting system (CIDR). Since 2017, HIV epidemiological data from CIDR are linked to HIVDR data provided by the National Virus Reference Laboratory (NVRL), in order to produce national TDR prevalence rates. This work is overseen by a national steering group (see Appendix 1 for membership).

Methods

Criteria for inclusion in surveillance

The criteria for inclusion in HIVDR surveillance are: a person aged ≥18 years, tested prior to commencing their first antiretroviral treatment (ART) regimen in Ireland for susceptibility to any of the 22 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.

Prior exposure to antiretroviral treatment

Of all individuals diagnosed with HIV in Ireland, a high proportion (42% in 2018) were previously diagnosed with HIV abroad, with the majority of those (88% in 2018) previously exposed to ART (5). Information on prior ART is recorded on HIV enhanced surveillance forms, which are completed by the practice or clinic where HIV is diagnosed (or the referral clinic) and provided to Departments of Public Health who enter data onto CIDR. Data for this report were extracted from CIDR on 25th September 2019. ART refers to treatment of HIV infection and does not include pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP).

Genotypic antiretroviral resistance testing (GART)

The NVRL undertakes all genotypic antiretroviral resistance testing (GART) in Ireland. GART was performed using nested RT-PCR and Sanger sequencing, drug resistance mutations (DRMs) were identified using Stanford University software (HIVdb algorithm versions 8.4-8.8) (6).

Sequencing was performed for 51% (n=266) of HIV diagnoses in 2018. For the remainder, sequencing was not performed due to either low viral load (n=228), a consequence of being on treatment at time of first diagnosis in Ireland, or because there was no suitable sample for

analysis (n=26). For three cases the CIDR event ID could not be linked to a laboratory sample number.

Of the 266 HIV diagnoses, integrase sequences could be generated for 262 persons, and could not be generated for four.

Genotypic definition of transmitted HIV-1 drug resistance

To compare TDR rates across geographic regions and times, WHO recommended in 2009 the adoption of a consensus genotypic definition of transmitted HIV-1 drug resistance, comprising a list of 93 RT/PR surveillance drug resistance mutations (SDRMs) (7). In 2019 a list of 24 non-polymorphic INSTI-selected mutations for quantifying INSTI-related TDR was published for the first time (8). In this study TDR was defined as the presence in ART-naïve individuals of one of more mutations from the WHO 2009 surveillance list or the 2019 INSTI SDRM list.

TDR can be both underestimated and overestimated when using the WHO 2009 surveillance list to categorise drug resistance. Underestimation of TDR may arise due to the omission of relevant mutations identified since 2009. Overestimation may arise from the inclusion of mutations that confer resistance to some drugs no longer recommended for first line therapy. It is hoped that an updated SDRM list will be published by WHO in the near future.

Statistical analysis

Ninety-five percent confidence intervals (CI) were computed using the Wilson score interval for binomial proportions, with OpenEpi software (9). CIs for TDR prevalence during the period 2004-2008 were computed using data from a separate study on documented prevalence of HIV type 1 antiretroviral TDR in Ireland from 2004 to 2008, CIs for 2015, 2016, and 2017 were calculated using data from annual reports (10-13).

Results

Prior exposure to antiretroviral treatment

Completeness of information on prior exposure to ART by suitability for sequencing is presented in Appendix 2. Of 523 HIV diagnoses in 2018, history of exposure to ART was available for 82% (n=430). Of these, 53% (n=227) were ART-naïve, 47% (n=203) were ART-experienced.

Transmitted HIV drug resistance

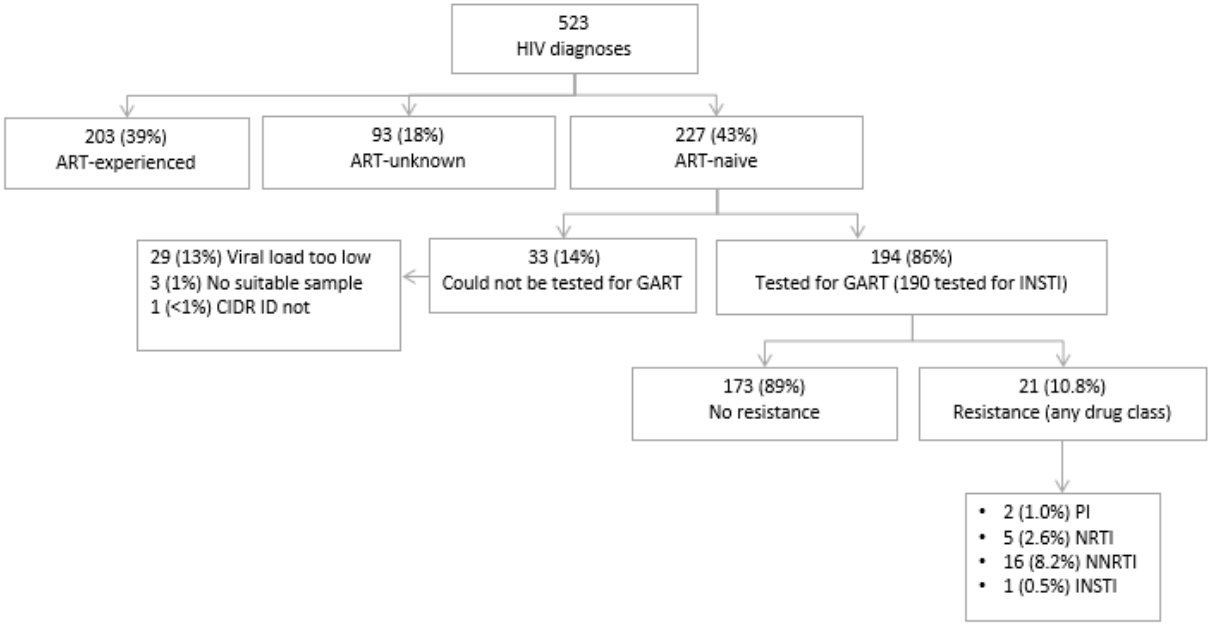
Sequencing was performed for 86% (n=194) of ART-naïve individuals diagnosed in 2018. Of those, 21 had one or more mutations from the 2009 surveillance list or the 2019 INSTI surveillance list, a TDR prevalence of 11% (CI 7.2% – 16.0%). Eighteen people had resistance to one drug class and three had resistance to two drug classes (Table 1). By drug class, resistance to NNRTIs (8%; CI 5.1% – 13.0%) was significantly higher than resistance to PIs (1%; CI 0.3% – 3.7%) and INSTIs (0.5% CI; 0.1% – 2.9%), but was not significantly different to resistance to NRTIs (3%; CI 1.1% – 5.9%).

Table 1 Number of individuals with drug resistance mutations (WHO 2009 surveillance list or 2019 INSTI surveillance list), by drug class and history of prior exposure to ART, Ireland, 2018

	ART-experienced	ART-naïve	ART-unknown	Total
PI	0	1	1	2
NRTI	0	2	1	3
NNRTI	5	14	6	25
PI+NRTI	0	1	2	3
NRTI+NNRTI	1	2	0	3
INSTI	0	1	0	1
Total	6	21	10	37

Figure 1 presents the categorisation of TDR cases. A list of surveillance drug resistance mutations (SDRMs) by HIV subtype is presented in Appendix 3.

Figure 1 Categorisation of transmitted HIV drug resistance (TDR), Ireland, 2018. (TDR defined as ≥1 mutation from WHO 2009 surveillance list or 2019 INSTI surveillance list)



Demographic characteristics

Table 2 presents the demographic characteristics of ART-naïve people tested and of those with TDR (any drug class) in 2018. Data should be interpreted with caution due to wide confidence intervals caused by the small sample size for some subgroups. By region of origin, TDR prevalence was 14% among people born in sub-Saharan Africa, 14% among people born in Latin America, and 9% among people born in Ireland. By probable route of transmission, TDR prevalence was 12% among heterosexual males and 11% among men who have sex with men (MSM).

Table 2 Demographic characteristics of ART-naïve population tested, and of those with transmitted HIV drug resistance (TDR), Ireland, 2018. (TDR defined as ≥1 mutation from WHO 2009 surveillance list or 2019 INSTI surveillance list)

		Total ART-naïve population tested	Individuals with SDRMs	Prevalence of TDR	95% CI	
		N	N	%		
Total		194	21	10.8	7.2	16.0
Sex	Male	159	18	11.3	7.3	17.2
	Female	35	3	8.6	3.0	22.4
Age group (years)	0-14	1	0	0.0	-	-
	15-24	15	2	13.3	3.7	37.9
	25-34	80	9	11.3	6.0	20.0
	35-44	52	4	7.7	3.0	18.2
	45+	46	6	13.0	6.1	25.7
Region of origin	Ireland	68	6	8.8	4.1	17.9
	Sub-Saharan Africa	49	7	14.3	7.1	26.7
	Latin America	35	5	14.3	6.3	29.4
	Europe	29	1	3.4	0.6	17.2
	North America	3	2	66.7	20.8	93.9
	Other /Unknown	10	0	0.0	-	-
Probable route of transmission	MSM/bisexual male	103	11	10.7	6.1	18.1
	Heterosexual male	42	5	11.9	5.2	25.0
	Heterosexual female	33	3	9.1	3.1	23.6
	People who inject drugs	9	2	22.2	6.3	54.7
	Other /Unknown	7	0	0.0	-	-
Median CD4 count* (range)		315 (0-1290)	331 (6-665)			
Subtype	B	71	10	14.1	7.8	24.0
	C	49	4	8.2	3.2	19.2
	CRF02_AG	22	3	13.6	4.7	33.3
	A	14	2	14.3	4.0	39.9
	F	4	1	25.0	4.6	69.9
	D	2	1	50.0	9.5	90.6
	Other**	32	0	0.0	-	-

*CD4 count was unknown for 23 (12%) ART-naïve people tested, and for three (14%) people with TDR
**Subtypes CRF01_AE, CRF12_BF, CRF06_cpx, G

Table 3 presents the demographic characteristics of people with TDR by drug class. PI related TDR (n=2) and INSTI related TDR (n=1) were detected in Irish-born MSM only.

Table 3 Transmitted HIV drug resistance (TDR) by demographic characteristics and drug class, Ireland, 2018 (TDR defined as ≥1 mutation from WHO 2009 surveillance list or 2019 INSTI surveillance list)

Males (n=18)

		PI	NRTI	NNRTI	PI+NRTI	NRTI+NNRTI	INSTI
Age group (years)	15-24		1	1			
	25-34			6	1		
	35-44	1		2			
	45+		1	3		1	1
Region of origin	Ireland	1	2	1	1		1
	Sub-Saharan Africa			3		1	
	Latin America			5			
	North America			2			
	Europe			1			
Probable mode of transmission	MSM/bisexual	1	2	6	1		1
	Heterosexual			4		1	
	PWID			2			

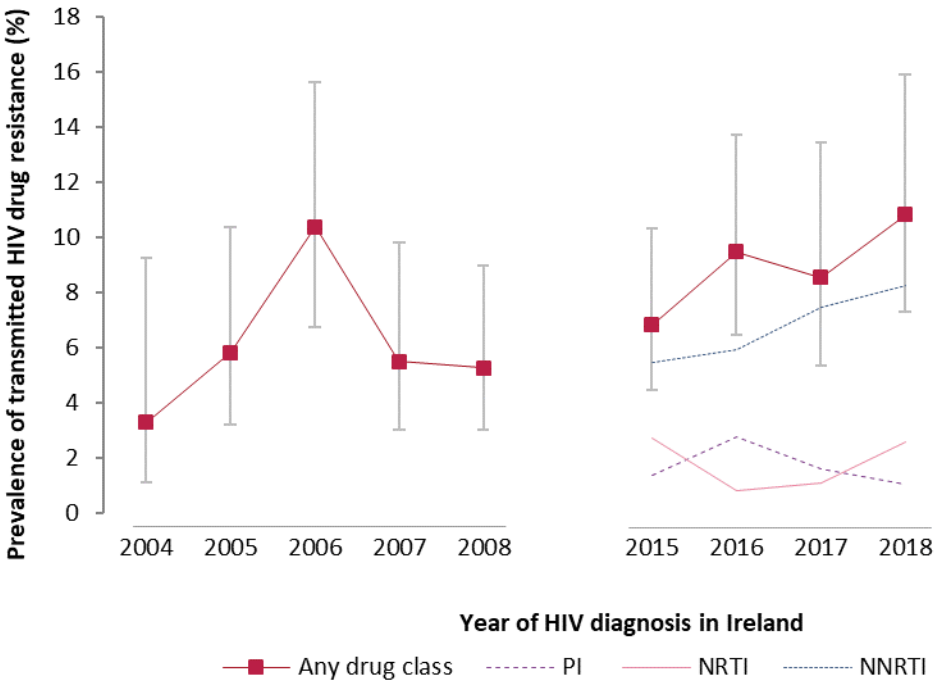
Females (n=3)

		NNRTI	NRTI+NNRTI
Age group (years)	25-34	1	1
	35-44	1	
Region of origin	Sub-Saharan Africa	2	1
Probable mode of transmission	Heterosexual	2	1

Trends

The available data on trends in TDR in Ireland are shown in Figure 2. Trends should be interpreted with caution due to the different methods used over time to define TDR and history of prior exposure to ART (10-13).

Figure 2 Prevalence (%) and 95% confidence intervals of transmitted HIV drug resistance (TDR) in Ireland, 2004-2008 and 2015-2018. Prevalence for 2004 to 2016 was calculated using different methods and may not be compared reliably with 2017 or 2018 data.



Transmitted HIV drug resistance among people with recent infection

Data on the recency of HIV diagnoses in Ireland were used to estimate the prevalence of TDR among people likely recently infected (within 4 months prior to testing). Of 523 people diagnosed with HIV in 2018, 54 (10%) were likely recently infected, categorised using the Recent Infection Testing Algorithm (RITA) or a p24 antigen positive status (14).

Of those who were likely recently infected, 76% (n=41) were ART-naïve and 24% (n=13) were ART-unknown. HIVDR testing was performed for 95% (n=39) of people who were ART-naïve; three had one or more mutations from the 2009 surveillance list or the 2019 INSTI surveillance list, corresponding to a TDR prevalence of 8% (95% CI 2.7% - 20.3%). All three people had resistance to one drug class only. By drug class, TDR prevalence was 5% (n=2) for NNRTIs and 3% (n=1) for PIs. A list of SDRMs by HIV subtype is presented in Appendix 4.

European-Level Surveillance of HIV Drug Resistance

European-level surveillance of HIVDR was commenced by the European Centre for Disease Prevention and Control (ECDC) in 2019, for 2018 and historical data. The criteria for inclusion in surveillance was defined as any newly diagnosed treatment-naïve HIV patient tested prior to initiating HIV treatment for susceptibility to any of the 22 available antiretroviral drugs in the four main drug classes. HIVDR was defined as any mutation or combination of mutations that produces low, intermediate or high-level resistance to any relevant NRTI, NNRTI, PI or INSTI (15). Levels of resistance were determined using the Stanford HIV Drug Resistance Database HIVdb. Data on HIVDR in Ireland in 2018 were submitted to the European Surveillance System (TESSy) in 2019; results of European-level TDR surveillance are not yet published but results for Ireland (using the ECDC categorisation of HIV drug resistance) are shown in Appendix 5.

Discussion

The prevalence of TDR in Ireland was 11% in 2018, an increase from 9% in 2017 (this increase was not statistically significant).

By drug class, the prevalence of NNRTI-related TDR was 8%; this was equal to the prevalence of NNRTI-related TDR in 2017. The prevalence of PI-related TDR was 1% in 2018, a decrease from 2% in 2017. The prevalence of NRTI-related TDR was 3%, an increase from 1% in 2017. One person had INSTI-related TDR in 2018 (a prevalence of 0.5%), compared to none in 2017.

By region of birth, prevalence of TDR was higher among some subgroups, including people born in sub-Saharan Africa (14%) and people born in Latin America (14%), but the difference in TDR prevalence among regions was not statistically significant. By probable route of transmission, TDR prevalence was highest among heterosexual males (11%), an increase from the prevalence in 2017 (3%), but this increase was not statistically significant (13). Prevalence of TDR among MSM was 10%, similar to 2017 (9%), and it was 9% among heterosexual females, similar to 2017 (8%).

Latest data on HIV drug resistance in the United Kingdom shows a TDR prevalence of 10% (any-drug class), based on the WHO 2009 SDRM categorisation (16). European-level data are not yet available, but it is expected that a report will be published in the near future. The WHO reports data on PDR in low and middle income countries (LMIC) (1). Latest survey data from 2014 to 2018 shows high levels (>10%) of NNRTI-related PDR (resistance to efavirenz and/or nevirapine) among adults initiating first-line ART in 12 of 18 LMICs. PDR was higher in specific subpopulations, such as females, and people reinitiating first-line ART following previous exposure. PDR is not currently monitored in Ireland as data on treatment interruption are not currently collected.

Limitations to surveillance of HIV drug resistance in Ireland include that information on history of exposure to ART is not available for all cases. Those without information on prior ART are excluded from analysis which may result in underestimation of TDR. Furthermore, not all cases are suitable for HIV drug resistance testing. In 2018 this was mostly due to samples with low

viral loads, suggesting viral suppression due to already being on antiretroviral treatment. Whilst it may be possible to perform proviral DNA sequencing in these individuals to identify latent HIVDR, it will not be possible to ascertain whether any resistance identified in the provirus constitutes TDR or ADR. Sensitivity of testing might improve in future years with the planned introduction of next generation sequencing at NVRL. Limitations of demographic analyses include that testing biases may exist due to better testing access and uptake among some subgroups.
The WHO 2009 surveillance list in combination with the 2019 INSTI SDRM list were used to categorise HIV drug resistance in this study. Use of the WHO 2009 list can result in under estimation or in overestimation of TDR, due to reasons previously described. It is hoped that an updated surveillance list for NNRTI, NRTI and PI associated TDR will be published by the WHO in the near future. Other available methods to categorise HIV drug resistance include using the scoring system in the Stanford HIVdb algorithm but TDR prevalence can be largely overestimated using this method.

Early engagement in care and immediate initiation of effective antiretroviral treatment are critical for clinical benefits to individuals and to prevent onward transmission of TDR; therefore data from this report, and continuation of TDR surveillance in future, may be helpful to guide development of national treatment guidelines, or indeed preferred medicine strategies for the management of HIV. This study does not include TDR prevalence to individual drug level; including this information will be considered for future reports.

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Report prepared by

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Appendices

Appendix 1 Membership of the Developments in HIV Surveillance Steering Group in 2018/2019 (when these data were being collected/analysed). Membership list does not reflect changes to the group since 2019.

Name	Organisation
Derval Igoe (chair)	HSE Health Protection Surveillance Centre
Melissa Brady	HSE Health Protection Surveillance Centre
Kate O'Donnell	HSE Health Protection Surveillance Centre
Jeff Connell	National Virus Reference Laboratory
Cillian De Gascun	National Virus Reference Laboratory
Suzie Coughlan	National Virus Reference Laboratory
Martha Neary	National Virus Reference Laboratory
Joanne Moran	National Virus Reference Laboratory and HSE Health Protection Surveillance Centre
Sarah Doyle	Public Health STI HIV Special Interest Group
Orla Ennis	Public Health STI HIV Special Interest Group
Fionnuala Cooney	Public Health STI HIV Special Interest Group
Shay Keating	Society for the Study of Sexually Transmitted Diseases in Ireland
Erin Nugent	HIV Ireland (formerly Dublin AIDS alliance)
Siobhan O'Dea	Gay Men's Health Service
Lysander Preston	Positive Now
Helen Tuite	Infectious Disease Society of Ireland and Society for the Study of Sexually Transmitted Diseases in Ireland
Fiona Lyons	Infectious Disease Society of Ireland and Society for the Study of Sexually Transmitted Diseases in Ireland
Caroline Hurley	HSE Sexual Health and Crisis Pregnancy Programme

Appendix 2 History of exposure to antiretroviral treatment, by GART suitability, HIV diagnoses, 2018, Ireland

Previously exposed to antiretroviral treatment?	All		Tested for GART		Not tested for GART	
	n	%	n	%	n	%
Yes	203	38.8	21	7.9	182	70.8
No	227	43.4	194	72.9	33	12.8
Unknown	93	17.8	51	19.2	42	16.3

Appendix 3 Surveillance drug resistance mutations among ART-naïve people tested for HIV drug resistance, by HIV-1 subtype, Ireland, 2018 (mutations from the WHO 2009 surveillance list and WHO 2019 INSTI surveillance list).

	All	A	B	C	CRF02_AG	D	F
Number of ART-naïve individuals tested NRTI/NNRTI/PI*	194	14	71	49	22	2	4
Number of ART-naïve individuals tested INSTI*	190	14	70	47	22	2	4
Number of ART-naïve individuals with SDRMs (any drug class)	21	2	10	4	3	1	1
PI mutations (n=3)							
D30N	1		1				
M46L	1		1				
N88D	1		1				
NRTI mutations (n=9)							
D67E	1				1		
K219Q	1		1				
K65R	1		1				
M41L	1		1				
M184V	1	1					
T215D	1		1				
T215F	1	1					
T215S	1				1		
T69S_SG	1				1		
NNRTI mutations (n=21)							
G190A	2		1		1		
G190S	1	1					
K101E	4			2	1	1	
K103N	7		4	1	1		1
K103S	3		2	1			
P225H	1				1		
V106M	1			1			
Y181C	2	1			1		
INSTI mutations (n=1)							
R263K	1		1				
Total number of surveillance drug resistance mutations	34	4	15	5	8	1	1

*Excludes HIV-1 subtypes CRF01_AE, CRF06_cpx, CRF12_BF, CRF60_BC, G, as there were no SDRMs detected among ART-naïve individuals with these subtypes

Appendix 4 Surveillance drug resistance mutations among ART-naïve people with likely recent HIV infection tested for HIV drug resistance, by HIV-1 subtype, Ireland, 2018 (mutations from the WHO 2009 surveillance list and WHO 2019 INSTI surveillance list).

	All	B	CRF02_AG
Number of ART-naïve individuals (likely recent infection) with SDRMs (any drug class)	3	2	1
PI mutations (n=1)			
M46L	1	1	
NNRTI mutations (n=3)			
K103N	2	1	1
K103S	1	1	
Total number of surveillance drug resistance mutations	4	3	1

Appendix 5 European-Level Surveillance of HIV Drug Resistance

Data on HIVDR in Ireland in 2018 were submitted to the European Surveillance System (TESSy) in 2019 (the EU-level report is not yet published). The EU-level surveillance protocol uses the Stanford HIVdb to categorise HIV drug resistance. The Stanford HIVdb is an online bioinformatics tool (https://hivdb.stanford.edu) that uses a clinical algorithm to analyse drug resistance data and is primarily used for individual patient management. It returns inferred levels of resistance to the most commonly used protease, nucleoside, non-nucleoside, and integrase inhibitors. Benefits of the algorithm include that it is updated frequently and that it includes recently identified surveillance drug resistance mutations, unlike the WHO 2009 surveillance list. Drawbacks include that it also includes drug resistance mutations that do not meet the criteria for TDR surveillance, and that are not clinically relevant in terms of first line treatment options. Therefore TDR prevalence can be overestimated.

Using the EU-level surveillance protocol to categorise drug resistance in Ireland in 2018, 37 ART-naïve individuals were identified with low, intermediate or high-level resistance to at least one drug class, a prevalence of 19% (CI 14.2% - 25.2%). Table 5a presents the frequency of resistance by drug class and prior exposure to ART.

Of the 37 individuals who were ART-naïve, 31 had resistance to one drug class and six had resistance to two drug classes. Resistance to NNRTIs was highest (16%; CI 11.1% - 21.2%) and was significantly higher than resistance to PIs (3%; CI 1.4% - 6.6%), NRTIs (2%; CI 0.8% - 5.2%), and INSTIs (2%; CI 0.5% – 4.4%).

Table 5a Number of individuals with low, intermediate or high-level HIV drug resistance mutations (from Stanford University HIVdb susceptibility algorithm), by drug class and prior exposure to ART, Ireland, 2018

	All	ART-naïve	ART-experienced	ART-unknown
PI	6	3	1	2
NRTI	1	0	0	1
NNRTI	40	25	6	9
INSTI	3	3	0	0
PI+NRTI	2	1	0	1
PI+NNRTI	2	2	0	0
PI+NRTI+NNRTI	1	0	0	1
NRTI+NNRTI	4	3	1	0
Total	59	37	8	14

Table 5b shows the list of drug resistance mutations detected in all individuals (regardless of prior exposure to ART), by HIV subtype. Table 5b shows the list of drug resistance mutations detected in people who were ART-naïve, by HIV subtype.

Drug resistant mutations detected by the Stanford HIVdb algorithm and that are categorised as resistant according to the ECDC definition, but that do not meet the criteria for TDR surveillance

according to the WHO consensus definition, mostly include NNRTIs that confer low level resistance, such as E138A, E138G, H221Y, and V108I.

Demographic characteristics

The median age among ART-naïve individuals with drug resistance mutations was 36 years (range 21-71 years); among males it was 39 (range 22-71 years) and among females it was 36 years (range 21-40 years).

By region of origin, prevalence of drug resistance mutations among ART-naïve persons was 25% among persons born in sub-Saharan Africa, 23% among persons born in Latin America, and 15% among persons born in Ireland.

By probable route of transmission, prevalence of drug resistance mutations among ART-naïve persons was 29% among heterosexual males, 18% among heterosexual females, and 15% among MSM.

Appendix 5b Drug resistance mutations among all individuals tested for HIV drug resistance, by HIV-1 subtype, Ireland, 2018 (low, intermediate or high-level resistance as categorised by the Stanford University HIVdb susceptibility algorithm)

	All	A	B	C	CRF02_AG	D	F	G
Number of individuals tested NRTI/NNRTI/PI*	266	16	105	69	29	2	6	12
Number of individuals tested INSTI*	262	16	104	67	29	2	6	12
Number of individuals with DRMs (any drug class)	59	2	21	22	7	1	5	1
PI mutations (n=10)								
D30N	2		2					
I47V	1			1				
I54M	1			1				
L10F	1		1					
M46L	1		1					
M46V	1		1					
N88D	2		2					
Q58E	1		1					
NRTI mutations (n=18)								
D67N	2			2				
K65R	1		1					
K70E	1			1				
K70R	1			1				
M184V	3	1		2				
M41L	3		3					
T215D	2		2					
T215E	1		1					
T215F	1	1						
T215S	2		2					
T69S_SG	1				1			
NNRTI mutations (n=73)								
A98G	2			1	1			
E138A	18		2	11	1		4	
E138G	2				2			
F227L	1			1				
G190A	3		1	1	1			
G190S	1	1						
H221Y	2		1		1			
K101E	4			2	1	1		
K101H	1			1				
K101P	1			1				
K103N	17		7	5	2		2	1
K103S	4		2	2				
K238T	1				1			
P225H	2				2			
V106I	3		1	1			1	
V106M	3			3				
V108I	2			1	1			
Y181C	3	1		1	1			
Y188H	1			1				
Y188F	1			1				
Y188L	1			1				
INSTI mutations (n=3)								
G163K	1						1	

G163R	1		1					
R263K	1		1					
Total number of drug resistance mutations	104	4	33	42	15	1	8	1

*Excludes HIV-1 subtypes CRF01_AE, CRF06_cpx, CRF12_BF, CRF60_BC, as there were no DRMs detected among individuals with these subtypes

Appendix 5c Drug resistance mutations among ART-naïve individuals tested for HIV drug resistance, by HIV-1 subtype, Ireland, 2018 (low, intermediate or high-level resistance as categorised using the Stanford University HIVdb susceptibility algorithm)

	All	A	B	C	CRF02_AG	D	F
Number of ART-naïve individuals tested NRTI/NNRTI/PI	194	14	71	49	22	2	4
Number of ART-naïve individuals tested INSTI	190	14	70	47	22	2	4
Number of ART-naïve individuals with DRMs (any drug class)	37	2	14	12	5	1	3
PI mutations (n=7)							
D30N	1		1				
M46L	1		1				
M46V	1		1				
N88D	1		1				
Q58E	3		1	2			
NRTI mutations (n=7)							
K65R	1		1				
M41L	1		1				
M184V	1	1					
T69S_SG	1				1		
T215D	1		1				
T215F	1	1					
T215S	1				1		
NNRTI mutations (n=42)							
A98G	1				1		
E138A	12		1	8	1		2
E138G	2				2		
G190A	2		1		1		
G190S	1	1					
H221Y	2		1		1		
K101E	4			2	1	1	
K103N	7		4	1	1		1
K103S	3		2	1			
K238T	1				1		
P225H	1				1		
V106I	2		1	1			
V106M	1			1			
V108I	1				1		
Y181C	2	1			1		
INSTI mutations (n=3)							
R263K	1		1				
G163K	1						1
G163R	1		1				
Total number of drug resistance mutations	59	4	20	16	14	1	4