



Public health surveillance of transmitted HIV drug resistance & subtype

The Kirby Institute at the University of New South Wales coordinates national HIV surveillance on behalf of the Australian Government Department of Health and in cooperation with State and Territory Governments. Public health HIV surveillance refers to the systematic collection and analysis of data relating to HIV at a population level. These data are used to guide the public health response to HIV prevention and treatment. Key data on HIV diagnoses are reported every year in the Annual Surveillance Report of HIV, viral Hepatitis and sexually transmissible infections published by the Kirby Institute.

The medical and public health response to HIV has evolved rapidly in recent years. These changes include:

- 1) An increased focus on providing treatment to people immediately after they are first diagnosed with HIV. Starting HIV treatment early has been shown to improve a person's health, including in the long term, compared with starting treatment laterⁱ. Also, starting treatment early, will quickly reduce the levels of HIV in the blood to a point where it can't be detected by testingⁱⁱ. When the HIV virus cannot be detected in the blood, the likelihood of transmission to another person is zero. This strategy is also referred to as treatment as prevention (TaSP).
- 2) The availability of subsidised HIV pre-exposure prophylaxis (PrEP) through the Pharmaceutical Benefits Scheme (PBS) for people who are at a medium to high risk of acquiring HIV. Taking PrEP as directed prevents the acquisition of HIV^{iii,iv}.
- 3) A national commitment to the virtual elimination of new HIV infections^v.

The information collected as part of public health surveillance also needs to be revised periodically. This includes information on transmitted HIV antiretroviral drug resistance and information on the broad distribution of HIV subtypes.



Here, we explain the terms HIV antiretroviral drug resistance and subtype and provide answers to a few frequently asked questions regarding the public health surveillance of these indicators.

1. WHAT IS TRANSMITTED HIV DRUG RESISTANCE?

Transmitted drug resistance means that a newly acquired virus already contains mutations that may make it less responsive to commonly used antiretroviral drugs. When this happens, the treatment given to a person newly diagnosed with HIV may not work effectively or at all and they need to be switched to an alternative treatment. To help doctors select the most effective antiretroviral therapy for each person, HIV drug resistance testing is recommended for all patients prior to or shortly after starting antiretroviral therapy^{vi}.

2. HOW IS DRUG RESISTANCE DETERMINED?

When a person is first diagnosed with HIV, the treating doctor collects a blood sample and requests the laboratory conduct a test for drug resistance to check whether the person has a virus that contains drug resistance mutations. This involves the laboratory test 'reading' a number of gene regions responsible for viral replication which are also the key regions that antiretroviral drugs aim to disrupt. The mutations found are checked against an international list of mutations that are known to confer resistance to individual drugs or drug types.

3. WHAT ARE THE BENEFITS OF COLLECTING INFORMATION ON TRANSMITTED DRUG RESISTANCE?

Monitoring levels of drug resistance among people newly diagnosed with HIV at a population level provides an important snapshot of how well recommended HIV treatments are working and if any changes need to be made to current treatment recommendations^{vii}.



This is particularly important given the recent advances in expanding access to HIV treatment for all people living with HIV, including those ineligible for Medicare benefits, and the introduction of PrEP. The drugs used in PrEP are the same as the drugs commonly used in the treatment of people living with HIV. With an increasing number of HIV positive and HIV negative people taking antiretroviral drugs for treatment or prevention, surveillance of drug resistance is needed to identify emerging resistance early and adjust the guidelines for treatment and PrEP accordingly.

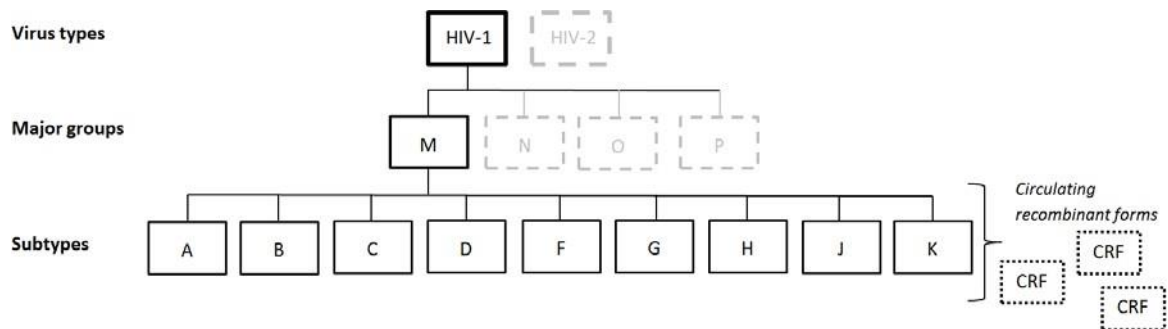
Resistance mutations can develop when antiretroviral treatment is interrupted, and a person's viral load is no longer undetectable. These resistance mutations can then be passed on with the virus. Increases in transmitted drug resistance may therefore also indicate a need for new and/or improved services to better support people living with HIV with adherence to their antiretroviral treatment.

4. WHAT IS A SUBTYPE?

A subtype is a category of HIV that groups similar virus strains together. Like other some other infectious diseases, HIV can be further broken down into different virus types and strains that have slightly different characteristics.

HIV is made up of two major virus types. HIV-1 is the most common type in Australia and is usually referred to simply as HIV. Within HIV-1, four broad groups are recognised, with the major group M being responsible for almost all HIV infections globally. The M group is further broken down into nine subtypes. The subtypes are denoted by one of the letters A, B, C, D, F, G, H, J, or K as shown below. When viruses belonging to different subtypes combine some of their genetic material, the resulting hybrid viruses are called 'circulating recombinant forms'. Different subtypes have distinct geographical origins. Most HIV infections in Australia, North America, and Western Europe involve subtype B, whereas subtype C is most common globally. Figure 1 below shows the different classification levels.

Figure 1: Classification of HIV



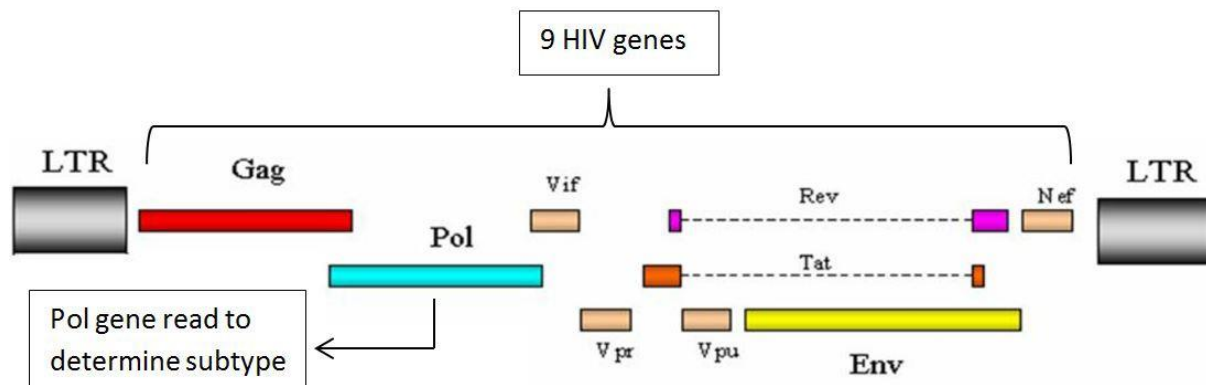
5. HOW IS SUBTYPE DETERMINED AND HOW IS IT DIFFERENT FROM GENOTYPE?

Subtype can be determined based on the same blood sample used to determine drug resistance mutations. Like testing for drug resistance, the process involves reading part of the virus' genes.

Each gene contains sequences of information that allow the virus to carry out particular functions, for instance the different steps needed for viral replication. Together, these genes make up the HIV genome. The genotype refers to the gene sequence that determines the characteristics that distinguish one virus from another virus. Genotypes can be determined for a particular gene or gene region but can also involve reading of a much larger part of the HIV genome.

The classification into subtypes requires reading of only a portion of the *polymerase (pol)* gene. For public health surveillance purposes at the national level, only the letter representing the subtype is reported. Subtype information is too broad to determine relationships between the viruses that different individuals are living with. This means that even if two people are reported as having the same rare subtype, there is not enough information to be able to link these two people by comparing their subtype information.

Figure 2: Genomic organisation of HIV



Adapted from: Rivera DM. Pediatric HIV Infection. Medscape. 2017. Available from: <https://emedicine.medscape.com/article/965086-overview>.

6. WHAT ARE THE BENEFITS OF COLLECTING INFORMATION ON SUBTYPE?

An understanding of the distribution of HIV subtypes in Australia is important to inform HIV management guidelines. There is evidence to suggest that the way HIV progresses in the body^{ix,x}, how the HIV virus responds to treatment, how it develops resistance mutations^{ix,xi,xii,xiii}, and the accuracy of viral load tests^{xiv} can all vary between different subtypes.

Also, changes in subtype distribution may indicate shifts in the demographics of people newly diagnosed with HIV. As described in section 4, some subtypes occur more commonly in certain parts of the world. Surveillance data on subtype distribution, combined with other demographic information of people diagnosed with HIV, including age, sex and cultural background, can help ensure that treatment and prevention strategies are tailored appropriately for those in need.

7. WHO HAS ACCESS TO DRUG RESISTANCE AND SUBTYPE INFORMATION?

Once laboratory tests have been conducted, the results are reported back to the treating doctor. As part of public health surveillance, laboratories will also report subtype and resistance information to state and territory health departments. The health departments oversee collecting health and demographic data related to HIV within their jurisdiction in accordance with the specific provisions

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of the public health legislation in their state or territory. The health departments then send the data to the Kirby Institute at the University of New South Wales for storage in the National HIV Registry.

All HIV subtype and resistance data are subject to the same privacy and confidentiality legislation as any other health and demographic data associated with HIV. This means that only authorised staff at laboratories, health departments, and the Kirby Institute have access to these data. In addition, HIV data stored at the national level use name codes consisting of the first two letters of the first name and the first two letters of the last name, rather than an individual's full name.

8. HOW ARE THE DRUG RESISTANCE AND SUBTYPE DATA COLLECTED FOR PUBLIC HEALTH SURVEILLANCE PURPOSES USED?

The primary use of these data is a national summary of drug resistance and subtype information provided by the Kirby Institute in its annual surveillance reports. These reports may be used to inform decisions about public policy, resource allocation for treatment and prevention, or clinical practice.

9. HOW DOES PUBLIC REPORTING PROTECT THE PRIVACY OF INDIVIDUALS AND COMMUNITIES?

Under no circumstances does public reporting of any data related to public health surveillance identify individuals. All public health data are reported in aggregated form, that is all cases that fit a particular category of interest are counted and reported in summary groups. In addition, all public reporting of drug resistance data is done in such a way that the potential for stigmatisation of specific population groups is minimised. Each annual surveillance report is reviewed by the Annual Surveillance Report Advisory Committee prior to publication. The committee includes members of community organisations that represent people and communities affected by HIV.

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