Public health surveillance of transmitted HIV drug resistance & subtype

The Kirby Institute at the University of New South Wales has been responsible for coordinating national HIV surveillance on behalf of the Australian Government Department of Health and in cooperation with the State and Territory Governments since 1986. Public health surveillance refers to the systematic collection and analysis of health data at a population level, in this case information related to diagnoses of HIV. The knowledge gained through surveillance activities is 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 antiretroviral treatment to people immediately after they are first diagnosed with HIV. Starting HIV treatment early has been shown to improve a person’s health compared with starting treatment later³.

2) Starting treatment for the purpose of preventing HIV as early, sustained treatment suppresses the virus to levels where it can’t be detected in a person’s blood⁴. When the virus is undetectable, the likelihood of transmission to another person is reduced to zero.

3) The establishment of HIV pre-exposure prophylaxis (PrEP) as an effective prevention strategy for individuals at high risk of acquiring HIV.³,⁴ PrEP involves HIV-negative persons taking HIV drugs and is highly effective at preventing transmission when taken as prescribed⁴ (also see section 3).

4) A national commitment to the virtual elimination of new HIV infections by 2020⁵.

With these changes, the information collected as part of public health surveillance also needs to be revised periodically. This includes information on transmitted HIV drug resistance, that is resistance to drugs that are commonly used in HIV treatment, and information on the broad distribution of HIV subtypes. Here, we explain the terms HIV 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 living with HIV may work poorly or not 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\textsuperscript{vi}.

2. **How is drug resistance determined?**

When a person is first diagnosed with HIV, their treating doctor collects a blood sample and requests the laboratory to 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 then 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 in Australia provides an important snapshot of how well the recommended HIV treatments are working and if any changes need to be made to current treatment recommendations\textsuperscript{vi}.

This is particularly important given the recent advances in expanding access to HIV treatment for all people living with HIV and the introduction of PrEP (pre-exposure prophylaxis). PrEP involves people who are HIV negative taking HIV antiviral treatments daily drugs to protect themselves from acquiring HIV\textsuperscript{viii}. The drugs that are taken for PrEP are the same ones that are commonly used in the treatment of people living with HIV. With an increasing number of HIV positive and HIV negative individuals being exposed to 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. This allows the resistant virus to start replicating again and the resistance mutations can then be passed on with the virus. Increases in transmitted drug resistance may therefore also indicate a need for services to better support people living with HIV with adherence to their antiretroviral treatment.

The type of information collected and how confidentiality is protected is described in section 8.

4. **What is a subtype?**

A subtype is a category of HIV that groups similar virus strains together. Like other infectious diseases, HIV can be further broken down into different virus types and strains that have slightly different characteristics. Figure 1 below shows the different classification levels: HIV is made up of two major virus types. HIV-1 is the most common type globally and 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, also known as clades. 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: 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. Similar to testing for drug resistance, the process involves reading part of the virus’ genes.

Figure 2 below shows that HIV is made up of nine genes. The entirety of the HIV genetic information is collectively known as the HIV genome. Each gene contains sequences of information that allow the virus to carry out particular functions, for instance the different steps needed for viral replication.

The genotype refers to the exact documentation of these sequences to determine the differences 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.

By contrast, the classification into subtypes requires reading of only a portion of the polymerase (pol) gene. When subtype is reported for routine public health surveillance purposes, only the letter denoting the subtype is reported. All data describing the exact make-up of the pol gene remain with the laboratories. Subtype information is too broad to determine relationships between the viruses that different individuals are living with. This means that even if two persons both have a rare subtype, they still belong to categories that are sufficiently broad as to not uniquely identify an individual’s viral strain.
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, how the HIV virus responds to treatment, how it develops resistance mutations, and the accuracy of viral load tests can all vary between different subtypes.

In addition, 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, can help ensure that treatment and prevention strategies are tailored specifically to the needs of these populations.

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 are in charge of collecting all data related to HIV notifications within their jurisdiction in accordance with the specific provisions of the public health legislation in their state or territory. They then send an agreed set of data on to the Kirby Institute which compiles a summary at the national level.

All HIV subtype and resistance data is subject to the same privacy and confidentiality legislation as any other information associated with HIV notifications. This means that only authorised staff at laboratories, health departments, and the Kirby Institute has access to these data. In addition, HIV
notifications use namecodes 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, at all stages of data collection, storage, and transfer.

8. **How are the 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 form. 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.


