MOLECULAR HIV SURVEILLANCE IN ALABAMA, 2010-2015

know. manage. live.

INTRODUCTION

Molecular HIV Surveillance (MHS), formerly referred to as Variant, Atypical, and Resistance HIV Surveillance (VARHS) is the analyses of the HIV-1 nucleotide sequences of viral genomes, which are used to identify the presence of mutations linked to antiretroviral (ARV) drug resistance. MHS provides a unique way of presenting community-level information to enhance prevention strategies, assess prevalence and trends in acquired and transmitted HIV drug resistance, guide public health actions such as ARV treatment, and increase the understanding of the burden of HIV in Alabama.

The objectives of MHS are as follows:

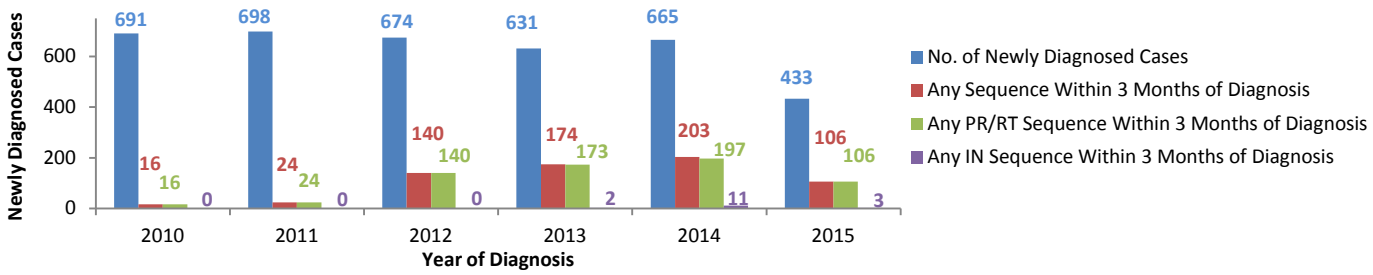
- Collect all HIV nucleotide sequence data from laboratories that perform HIV genotype drug resistance testing.
- Use molecular epidemiologic techniques to assess HIV drug resistance, evaluate HIV genetic diversity, and describe HIV transmission patterns.
- Disseminate results of molecular HIV data analyses to assist HIV treatment, prevention, and program planning and evaluation.

In December 2013, the Alabama Department of Public Health (ADPH) received funding from the Center for Disease Control and Prevention (CDC) to collect baseline viral genotype sequence data on newly diagnosed HIV positive individuals whose initial sequence was obtained within 3 months of HIV diagnosis. Alabama is fortunate to have the necessary laws in place that allow ADPH to collect genotype sequence data from both the State and private labs. After nearly two years of collaborating with multiple labs, ADPH now collects genotype sequence data via electronic lab reporting (ELR) from all major labs across the country. ADPH considers security and confidentiality a high priority for all Alabama residents and works diligently to ensure all HIV information is secure and in full compliance with the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention's (NCHHSTP) Data Security and Confidentiality Guidelines for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Programs: Standards to Facilitate Sharing and Use of Surveillance Data for Public Health Action.

HIV GENOTYPE COMPLETENESS IN ALABAMA

Alabama is a moderate morbidity state averaging 650 newly diagnosed HIV infections annually. HIV incidence surveillance data estimate an average of 760 new HIV infections occur in Alabama residents annually from 2010 to 2014, as one in six HIV-positive Alabama residents are unaware of their status. Figure 1 highlights the completeness of all HIV genotype sequences collected within three months of diagnosis from 2010 to 2015. As Alabama's MHS project was launched in December 2013, genotype reporting is considered complete beginning in 2014, with 2015 data remaining preliminary until December 31, 2016. Prior to 2014, limited, retrospective data are available from select laboratories. As additional laboratories transmit MHS genotype results to ADPH, data will continue to increase as new and retrospective genotype sequences are reported. Table 1 depicts demographics and HIV genotype completeness as of December 31, 2015.

Figure 1: Genotype Completeness in Alabama Within 3 Months of HIV Diagnosis, 2010-2015



Source: Alabama Department of Public Health, Division of STD Prevention and Control, HIV Surveillance Branch. Data accessed June 20, 2016.
Note: 2015 data is preliminary and remains incomplete due to delayed reporting; data will be finalized December 31, 2016.

Date of Report: 6/20/2016

know. manage. live.

Table 1. Completeness of HIV Sequences[€] Among Diagnosed Alabama Residents, 2010-2015

	Any Sequence				Any PR/RT Sequence[‡]				Any IN Sequence[£]				
	All		Within 3 Months of Diagnosis		All		Within 3 Months of Diagnosis		All		Within 3 Months of Diagnosis		Total Number of Diagnoses
	No.	%[†]	No.	%[†]	No.	%[†]	No.	%[†]	No.	%[†]	No.	%[†]	No.
Sex													
Male	718	24.5	509	17.3	710	24.2	505	17.2	18	0.6	11	0.4	2,934
Female	220	25.6	154	17.9	214	24.9	151	17.6	8	0.9	5	0.6	858
Age at Diagnosis													
<13	2	11.1	.	.	2	11.1	.	.	.	.	.	.	18
13-19	68	29.7	42	18.3	66	28.8	42	18.3	2	0.9	.	.	229
20-29	409	26.3	295	18.9	404	25.9	292	18.8	11	0.7	8	0.5	1,557
30-39	183	22.9	131	16.4	182	22.8	130	16.3	4	0.5	3	0.4	799
40-49	155	24.4	97	15.3	151	23.7	95	14.9	6	0.9	4	0.6	636
50-59	88	23.0	72	18.8	87	22.8	72	18.8	2	0.5	.	.	382
≥60	33	19.3	26	15.2	32	18.7	25	14.6	1	0.6	1	0.6	171
Race/Ethnicity													
Black	706	26.6	488	18.4	696	26.2	482	18.1	20	0.8	14	0.5	2,658
White	162	18.3	124	14.0	158	17.9	123	13.9	5	0.6	2	0.2	883
Hispanic	26	24.5	18	17.0	26	24.5	18	17.0	.	.	.	.	106
Multiple Races	41	32.3	30	23.6	41	32.3	30	23.6	1	0.8	.	.	127
Asian	3	27.3	3	27.3	3	27.3	3	27.3	.	.	.	.	11
Other/Unknown	.	.	.	.	.	.	.	.	.	.	.	.	7
Transmission													
Male													
MSM	510	26.4	373	19.3	504	26.0	370	19.1	12	0.6	6	0.3	1,935
IDU	10	34.5	8	27.6	10	34.5	8	27.6	.	.	.	.	29
MSM/IDU	18	32.1	8	14.3	18	32.1	8	14.3	.	.	.	.	56
Heterosexual	36	25.4	30	21.1	36	25.4	30	21.1	.	.	.	.	142
Other/Unknown	144	18.8	90	11.8	142	18.6	89	11.6	6	0.8	5	0.7	764
Female													
IDU	12	30.0	6	15.0	10	25.0	5	12.5	2	5.0	1	2.5	40
Heterosexual	106	30.8	80	23.3	106	30.8	80	23.3	1	0.3	1	0.3	344
Other/Unknown	100	21.6	68	14.7	96	20.7	66	14.2	5	1.1	3	0.6	464
Year of Diagnosis													
2010	90	13.0	16	2.3	87	12.6	16	2.3	3	0.4	.	.	691
2011	101	14.5	24	3.4	101	14.5	24	3.4	2	0.3	.	.	698
2012	194	28.8	140	20.8	193	28.6	140	20.8	1	0.1	.	.	674
2013	212	33.6	174	27.6	209	33.1	173	27.4	5	0.8	2	0.3	631
2014	233	35.0	203	30.5	226	34.0	197	29.6	12	1.8	11	1.7	665
2015	108	24.9	106	24.5	108	24.9	106	24.5	3	0.7	3	0.7	433
Total	**938**	**24.7**	**663**	**17.5**	**924**	**24.4**	**656**	**17.3**	**26**	**0.7**	**16**	**0.4**	**3,792**

Source: Alabama Department of Public Health, Division of STD Prevention and Control, HIV Surveillance Branch. Data accessed June 20, 2016.

Note: 2015 data is preliminary and remains incomplete due to delayed reporting; data will be finalized December 31, 2016.

Abbreviations: IDU – intravenous drug use, IN – integrase, MSM – men who have sex with men, PR – protease, RT – reverse transcriptase.

€ For persons with multiple sequences, the earliest and longest was selected. Excludes duplicate and invalid sequences.

‡ Sequence type can include PR/RT reported together, PR/RT/IN reported together, or PR and RT reported separately from the same specimen collection date.

£ Sequence type can include IN reported alone or PR/RT/IN reported together.

† Denominator = Total Number of Diagnoses.

TRANSMITTED DRUG-RESISTANT MUTATION (TDRM) BY DRUG CLASS

TDRM is classified on the basis of the CDC HIV-1 surveillance mutation list and the following criteria: the person has no evidence of prior ARV drug use and the nucleotide sequence is from a specimen that was collected within three months of the diagnostic specimen being collected. TDRM occurs in individuals who were infected with HIV and have a drug resistant mutation.

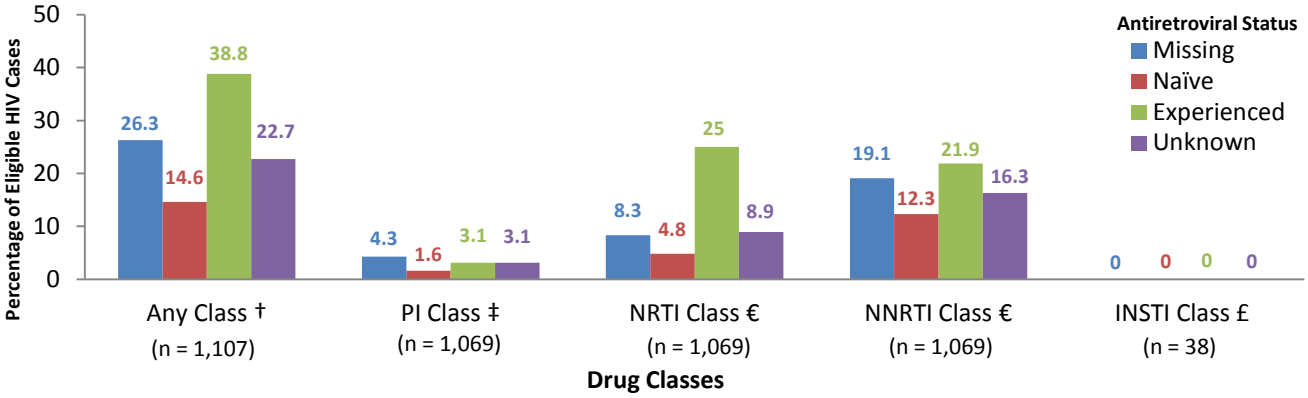
There are six major types of ARV drugs used to treat HIV: (1) protease inhibitors (PI), (2) reverse transcriptase inhibitors (nucleoside reverse transcriptase inhibitors (NRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI)), (3) integrase strand transfer inhibitors (INSTIs), (4) entry inhibitors, (5) fusion inhibitors, and (6) multi-class combination drugs. Each ARV drug acts against HIV via a specific method(s), with ARV drugs grouped by how they prevent HIV from replicating, thus decreasing the ability of HIV to invade, kill, take over, and reproduce itself in the body.

Protease inhibitors interfere with the protease enzyme HIV uses to cut long chains of itself into smaller individual proteins, preventing the assembly of new virus particles. NRTI and NNRTI inhibitors prevent the HIV enzyme reverse transcriptase (RT) from converting single-stranded HIV RNA into double-stranded viral DNA. INSTI inhibitors block the HIV integrase enzyme from infusing its genetic material into the genome of host cells with CD4 receptors. Entry inhibitors interfere with HIV's ability to bind to receptors on the outer surface of the cell, blocking entry into the cell at the attachment point. Similarly, fusion inhibitors interfere with HIV's ability to fuse with the cellular membrane, preventing HIV from entering the cell. Multi-class combination drugs combine HIV drugs from two or more classes, or types, into a single product.

Figure 2 shows the percentage of Alabama HIV cases from 2010 - 2015 with TDRM. Of all sequences (Any Class) of HIV cases, nearly 40 percent (38.8%) show evidence of TDRM among experienced ARV users. This indicates an interruption in or poor adherence to ARV medication(s). Poor adherence increases the risk of drug resistance, decreases the overall health and quality of life of an individual, and significantly increases the risk of transmitting HIV to others.

Fifteen percent of eligible cases experiencing TDRM to any class of ARVs were ARV naïve at the time of genotype sequence testing. This indicates the presence of HIV drug resistance mutation upon infection (i.e., the strain of HIV infecting these individuals was already resistant to one or more ARV medications). Prevention efforts should focus on routine monitoring of adherence to ARV and retention in care. It is important to notice that 49 percent of HIV cases with TDRM to any class of ARV have missing or unknown ARV history (26% and 23%, respectively).

Figure 2. HIV Cases with Transmitted Drug-Resistant Mutation by Antiretroviral (ARV) Status and Drug Class, 2010-2015



Source: Alabama Department of Public Health, Division of STD Prevention and Control, HIV Surveillance Branch. Data accessed June 20, 2016.
Note: The date the sequence was obtained is the date the specimen was collected for HIV genotype (resistance) testing. This table is limited to persons who resided in Alabama at diagnosis and were reported to CDC through December 2015. Persons with missing diagnosis years were excluded.
† Includes all sequences, not limited to one sequence per person or to baseline sequences or people without evidence of ARV use. Excludes duplicate and invalid sequences.
‡ Includes PR only, PR/RT and PR/RT/IN sequences that were able to be interpreted for the presence of PI class mutations.
€ Includes RT only, PR/RT and PR/RT/IN sequences that were able to be interpreted for the presence of NRTI & NNRTI class mutations.
£ Includes IN only and PR/RT/IN sequences that were able to be interpreted for the presence of INSTI class mutations.

HIV Subtype B and non-B subtype Categories

Small changes, also known as mutations, may occur each time HIV replicates in the body. This creates many different forms of HIV within the body of a single person living with HIV.

There are two types of HIV: HIV-1 and HIV-2. Both viruses have the same modes of transmission and can lead to acquired immune deficiency syndrome (AIDS). In the United States and worldwide, HIV-1 is the most common type of HIV infection. HIV-2 is most common in West Africa; however, there are some prevalent cases in other countries as well.

Of the three distinct HIV-1 groups M (major), O (outlier), and N (non-M/non-O), more than 90 percent of HIV-1 infections are classified as group M. Group O seems to be located only in west-central Africa. Group N, although rare, was discovered in Cameroon in 1998, and group P was discovered in Cameroon as well. Within group M HIV-1 infections, there are at least nine genetically related subtypes or clades: A, B, C, D, F, G, H, J and K.

Different subtypes may also combine genetic material within the cell of an HIV positive individual to form a new hybrid virus. If a new hybrid strain infects more than three people who do not have direct, epidemiologically linked infections, the subtype is known as a 'circulating recombinant form' (CRFs). One type of CRF (recombinant form) is a hybrid HIV strain created when two or more HIV strains of different subtypes are combined. Another CRF (unique recombinant form, or URF) is a hybrid strain resulting from the recombination of two or more HIV subtypes that have not been identified elsewhere.

Figure 3: Groups and Subtypes of HIV

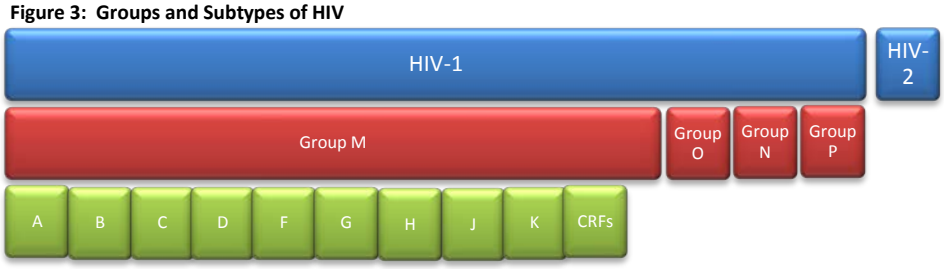
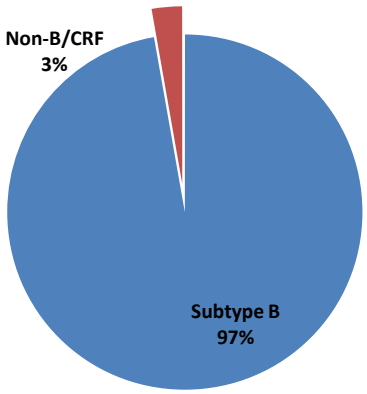


Figure 4 depicts two different subtype categories in Alabama: subtype B and non-subtype B/CRF. The subtypes are composed of all HIV cases with genotype sequence(s) reported to ADPH with a diagnosis year of 2010 to 2015.

Among the 938 Alabama residents with genotype sequences from 2010 – 2015), 96 percent of the cases were subtype B, while only 3 percent represent the other non-B and CRF subtypes, which were grouped together. This mirrors the national rate of 96 percent for subtype B and 4 percent for the other non-B and CRF subtypes, respectively. Therefore, unless specifically stated otherwise, subtype B is Alabama's focus going forward.

Figure 4: Subtypes among Alabama† Residents, 2010 - 2015 (n = 938)



Source: Alabama Department of Public Health, Division of STI Prevention and Control, HIV Surveillance Branch.

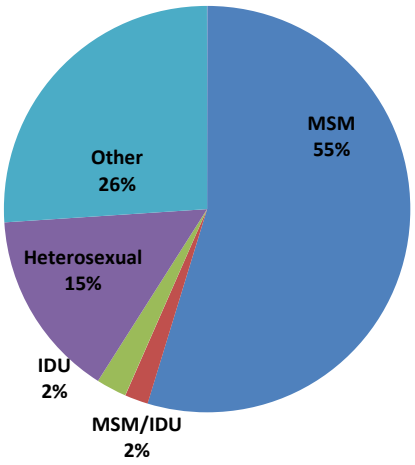
† Limited to persons who resided in Alabama at time of diagnosis.

Date of Report: 6/20/2016

HIV Subtype B Category by Mode of Transmission

Through observation over the years, certain subtypes/CRFs are predominantly associated with specific modes of transmission. Subtype B - the most common group M subtype of HIV-1 – is spread mostly by MSM contact and intravenous drug use (blood contact), while subtype C tend to spread among the heterosexual mode of transmission (mucosal route). In Alabama, Subtype B is the most common group M subtype of HIV-1.

Figure 5: Subtype B by Mode of Transmission in Alabama†, 2010 - 2015 (n = 910)



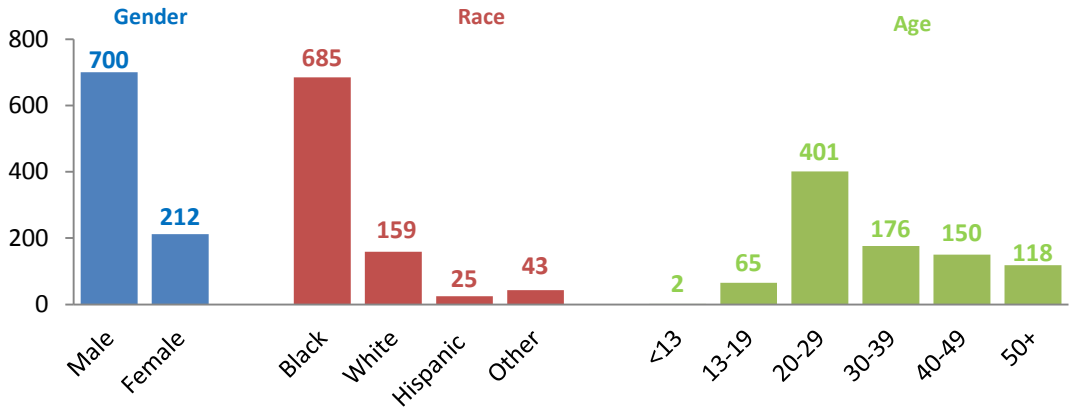
Source: Alabama Department of Public Health, Division of STI Prevention and Control, HIV Surveillance Branch.
† Limited to persons who resided in Alabama at time of diagnosis.

Figure 5 seems to follow the observation that subtype B is spread mostly by MSM contact. Alabama's MSM sub-population has the highest subtype B mode of transmission than any other category, comprising more cases than half (55%) of all newly diagnosed HIV cases. The other/unknown category is slightly more than one-fourth of the HIV subtype B population. Although the allocation of resources is limited, Alabama must be diligent to increase surveillance efforts and identify this important information, which will guide HIV intervention efforts and the allocation of funds for partnering organizations.

HIV Subtype B Category by Gender, Race and Age

As of December 31, 2015, among each demographic characteristic in Alabama (Figure 6), males (n = 700), Blacks (n = 685) and young adults 20 to 29 years of age (n = 401) each have a significantly higher count of Subtype B HIV cases in comparison to their counterparts in each subtype B group. In each category, males (77%) and Blacks (75%) represent approximately three quarters of the subtype B population, and young adults 20 to 29 years (44%) represent nearly half of all genotype subtype B HIV cases within the age category. This indicates males, Blacks, and young adults remain high risk target groups for HIV treatment and prevention efforts in Alabama. Without proper intervention, the percentage of subtype B infections among these groups will continue to rise.

Figure 6: Subtype B by Gender, Race, and Age in Alabama, 2010 - 2015 (n = 912)

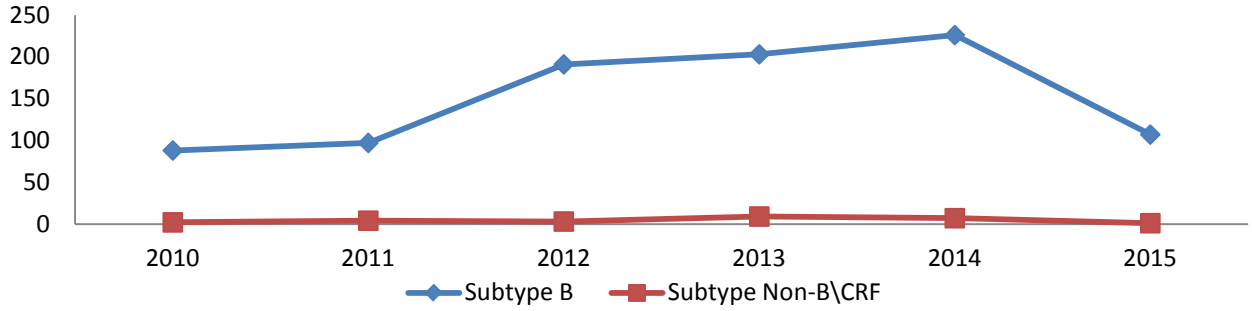


Source: Alabama Department of Public Health, Division of STI Prevention and Control, HIV Surveillance Branch.
† Limited to persons who resided in Alabama at time of diagnosis.

HIV Subtype B and non-B/CRF Categories by Year

Figure 7 depicts a six year time span in Alabama indicating the majority of newly diagnosed HIV infections with genotype results are subtype B, compared to non-B\CRF subtypes. This trend mirrors the national average, indicating that subtype B is the predominate subtype.

Figure 7: Subtype B and Non-B\CRF Categories by Years 2010 – 2015 in Alabama†

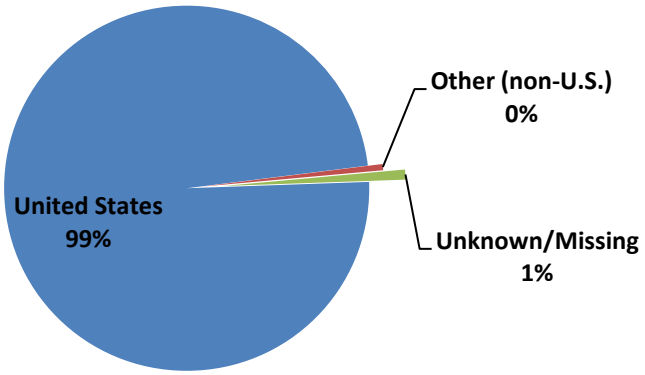


Source: Alabama Department of Public Health, Division of STI Prevention and Control, HIV Surveillance Branch.
Note: 2015 data is preliminary and remains incomplete due to delayed reporting; data will be finalized December 31, 2016.
† Limited to persons who resided in Alabama at time of diagnosis.

HIV Subtype B by Country of Birth

Nearly 100 percent of the genotyped subtype B individuals with HIV, who resided in Alabama at the time of diagnosis, were born in the United States. This indicates that the migration rate of people from areas of the world with non-B subtype relocating to Alabama is very low.

Figure 8: Percent of Subtype B by Country of Birth, and Residence at Diagnosis (n = 912)†



Source: Alabama Department of Public Health, Division of STI Prevention and Control, HIV Surveillance Branch.
† Limited to persons who resided in Alabama at time of diagnosis.

MHS activities support the National HIV/AIDS Strategy 2020 goals of: (1) reducing new HIV infections through the potential use of nucleotide sequence data to determine duration of infection for monitoring incidence; (2) increasing access to care and improving health outcomes by using nucleotide sequence data as a marker for linkage to, and quality of, care; and (3) reducing HIV-related disparities and health inequities by using nucleotide sequence data to reveal transmission patterns and provide insight into prevention.