

Research Brief

HIV/AIDS

MARCH 2015

Acquired Immunodeficiency Syndrome (AIDS) was first clinically recognized as a disease in 1981, although research has shown evidence of likely deaths in the United States from the disease as early as the 1950s (HIV In Site, 2014). AIDS develops from a viral infection affecting the immune system called the Human Immunodeficiency Virus (HIV), which was identified as the causative agent for AIDS in the mid-1980s.

When initially infected with HIV, individuals often experience flu-like symptoms while the virus replicates rapidly and spreads throughout the body triggering the immune system to activate and fight the infection. An asymptomatic period, averaging ten to twelve years in up to 70% of those infected, often follows. During that time, the HIV virus multiplies and accumulates in the blood stream and other organs. Eventually, the body's ability to fight infection and disease is destroyed, making the individual highly susceptible to opportunistic infections that would be less harmful in a healthy human body (National Institute of Allergy & Infectious Diseases [NIAID], 2009).

"HIV attacks the immune system by destroying CD4 positive (CD4+) T cells, a type of white blood cell that is vital to fighting off infection. The destruction of these cells leaves people infected with HIV vulnerable to other infections, diseases and other complications" (NIAID, 2009). The exact mechanism of how this occurs is a primary focus of AIDS research.

One recently reported study found that HIV causes CD4+T cell death primarily indirectly

rather than as a result of a cell invasion process as has been previously hypothesized. The virus attempts to invade CD4+T cells but fails. When this happens, the damage caused to the CD4+T cells activates an immune response that causes the cells to commit suicide in a process called pyroptosis, "a fiery and highly inflammatory form of cell death" (University of California San Francisco [UCSF], 2013). During this process, replacement cells are called to the site of the infection and subsequently undergo the same cycle, ultimately depleting the supply of CD4+T cells (UCSF, 2013).

The most advanced stages of HIV infection are characterized by symptoms of multiple opportunistic infections and a CD4+T cell count of less than 200 per cubic millimeter of blood (a normal, healthy range is 800-1,200 per cubic millimeter of blood). Once an HIV-infected person exhibits these indicators, he or she is officially diagnosed with AIDS (NIAID, 2009).

National Statistics

Since 1981, approximately 1.8 million people in the United States have been diagnosed with HIV or AIDS, including more than 650,000 people who have already died. The mortality rate peaked in 1995, when HIV was the leading cause of death for Americans ages 25 to 44 (Kaiser Family Foundation [KFF], 2014a). Since then, the mortality rate associated with HIV/AIDS has declined and it is currently the 6th leading cause of death for individuals ages 25 to 44 (World Health Organization [WHO], 2014). HIV rates of infection have also fallen dramatically from around 130,000 cases per year in the 1980s to

HIV/AIDS Research Brief March 2015

50,000 new cases per year today (KFF, 2014a). Current statistical estimates regarding the disease are as follows:

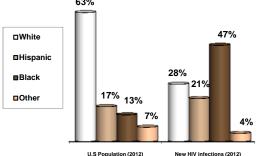
	_	New HIV diagnoses (2012)	47,746
	_	HIV Deaths (2011)	17,339
	_	AIDS Deaths (2011)	13,834
	_	People living with AIDS (2011	494,245
	_	People living with HIV (2011)	877,828
(C	en	ters for Disease Control and Prevention	[CDC], 2015)

Race/Ethnicity

AIDS affects minority populations

disproportionately. Minorities represented 72% of new HIV infections in 2012 and 70% of AIDS deaths in 2011 with African-Americans showing the largest disparity, making up only 13% of the total population but accounting for 47% of new HIV diagnoses (CDC, 2015).





(CDC, 2015; U.S. Census, 2015)

Sexuality

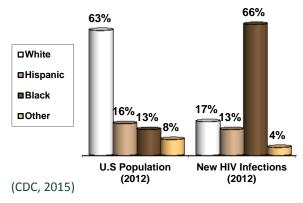
New infections have decreased among women but have increased among gay and bisexual men. While estimates show that men who have sex with men (MSM) comprise only 2% of the U.S. population, this group accounts for most new HIV infections (KFF, 2014a). In 2012 MSM comprised 64% of all new HIV infections in the U.S. Additionally, between 2010 and 2012, annual new HIV infections increased 14% among MSM (CDC, 2015).

Gender

There are approximately 280,000 women living with HIV/AIDS (24% of those infected) (KFF, 2014b). Imitating the national trend, minority women are disproportionately represented. Black women comprise the majority of women living with HIV, new infections, and AIDS

deaths. Incidence rates for new infections were almost 20 times higher for black women than white women in 2012. Overall, the incidence of new infections is on the decline, decreasing by 20% between 2008 and 2012 (CDC, 2015).

New HIV Infections Among Women U.S. Female Population, by Race/Ethnicty



Age

Teens and young adults under the age of 35 are considered at high risk for new HIV infections, constituting approximately 51% of new cases in 2012 and adolescent men (age 13-24) accounted for 1 in 5 new infections (CDC, 2015). During 2012, 13-24 year olds made up a greater share of newly infected blacks (27%) and Latinos (20%) than they did among newly infected whites (14%) (CDC, 2015). Most young people are infected sexually (KFF, 2014a).

Transmission of the HIV infection

The HIV infection can be transmitted through sexual contact, needles, blood transfusions using infected blood, exposure to the virus prior to or during the birth process, and occupational exposure (CDC, 2014a). During the two and a half decades spent tracking HIV/AIDS, incident rates have varied among the groups at highest risk for the disease, including men who have sex with men (MSM) and injecting drug users (IDU). The majority of women are infected through heterosexual sex. Though the incidence of perinatal infection has declined significantly due to the availability of antiretroviral treatment, transmission between HIV-infected pregnant women and their babies continues to take place. The majority of these

infections occur among African American women (KFF, 2014a).

Distribution of U.S. AIDS Cases by Transmission Exposure Group over Time					
Percent in Exposure Group				Group	
Exposure Group	2000	2005	2010	2012	
MSM	41%	45%	51%	52%	
IDU	26%	18%	13%	11%	
MSM IDU	6%	6%	5%	4%	
Heterosexual contact	26%	29%	31%	32%	
No risk identified/other	1%	1%	1%	1%	
(CDC, 2015)					

Regional Statistics

In 2012, Texas ranked ninth in the nation for the highest rate of newly reported HIV cases at 22.3 per 100,000 people (CDC, 2015). In 2013, Texas reported a new infection rate of 16.3 per 100,000 (Texas Department of State Health Services [DSHS], 2014c). There were over 76,000 people living with AIDS in Texas during 2013 and it is estimated that another 16,000 more could have the virus but be undiagnosed (DSHS, 2014a, p.2).

The following table outlines more recent HIV/AIDS statistics from the Texas Department of State Health Services for Texas, San Antonio, and the KCF counties of Interest.

2013 TEXAS HIV/AIDS SURVEILLANCE REPORT							
	Cumulative HIV/AIDS cases*	2013 HIV diagnoses		2013 AIDS diagnoses		Currently living with HIV/AIDS	
	Cases	Cases	Rate⁺	Cases	Rate⁺	Cases	Rate⁺
Texas	126,562	4,309	16.3	2,448	9.3	76,621	289.7
Male		3,501	27	1,900	14.5	59,922	455.8
Female		808	6	548	4.1	16,699	125.5
White		941	8	507	4.3	21,432	182.1
Black		1,656	52	983	31.0	27,352	880.0
Hispanic		1,527	15	845	8.3	21,447	215.3
Other		79	6	24	1.9		
Bandera	23	1	4.9	2	9.7	11	53.4
Bexar	8,641	380	20.9	160	9.1	4,727	260.1
Comal	157	8	6.8	3	2.7	100	84.4
Kendall	33	3	7.9	1	2.6	24	63.5

 $^{^{*}}$ Includes all reported since 1980, including cases originally reported as HIV which have progressed to AIDS

Prevention and Treatment

HIV testing is a crucial component of both prevention and treatment measures. Despite efforts to make testing more accessible, only 43.7% of individuals in the U.S. aged 18-64 reported ever having an HIV test in 2013. The percentage of those tested in Texas was similar at 43.5% (KFF, 2015a).

HIV/AIDS effect on patients has been greatly altered in the past decade due to innovative treatments. Drug treatments "lower the amount of HIV in the blood of infected persons, also called *viral load*, and successful treatment is known as viral suppression" (DSHS, 2014a, p.3).

The recommended treatment for HIV is called anti-retroviral therapy (ART) which consists of taking three or more medications from at least two of the six classes of FDA-approved drugs to treat HIV infection (U.S. Department of Health and Human Services [HHS], 2014). The classes of approved drugs include:

- Non-nucleoside reverse transcriptase inhibitors (NNRTIs) which bind to and alter reverse transcriptase the enzyme needed to convert viral RNA to DNA in preparation for reproduction
- 2. Nucleoside reverse transcriptase inhibitors (NRTIs) which *block reverse transcriptase*

[†] Rates represent cases per 100,000 population (DSHS, 2014c)

HIV/AIDS Research Brief March 2015

3. Protease inhibitors (PIs) *block protease*, an enzyme used to assemble viral proteins during the reproduction cycle

- 4. Fusion inhibitors *block HIV from entering* the CD4 cells of the immune system
- 5. CCR5 antagonists block HIV from entering the CD4 cell by *blocking needed protein*
- 6. Integrase inhibitors *block the enzyme* that hides the viral DNA in the cell nucleus

The first two classes of drugs help delay the spread of HIV and the onset of opportunistic infections by interrupting the early stages of virus reproduction, while protease inhibitors are designed to prevent the virus from copying itself, but work at later stages of the virus life cycle. Working to shield HIV from entering the cells, fusion inhibitors and CCR5 antagonists have been integral in the HIV treatment process and are designed to hinder HIV's ability to infect the body's immune system; additionally, integrase inhibitors have been used to disable the protein which HIV needs to cause an immune cell to produce new HIV cells (HHS, 2014; NIAID, 2009).

Although ART does not cure HIV/AIDS, it has been largely responsible for declines in AIDS diagnoses and deaths. Its effectiveness has given people with AIDS a longer lifespan and it has given HIV-infected persons the ability to live longer without developing AIDS (HHS, 2014). "Recent research has shown that persons with suppressed viral loads are also less likely to transmit the virus to others, making effective treatment a key prevention strategy" (DSHS, 2014a, p.3).

Despite its beneficial effects, ART is not an effective treatment for all cases of HIV/AIDS. It requires a consistent, long-term commitment and strict schedules of complicated medication combinations. There are many potential side effects associated with the use of antiviral treatment including liver damage, hyperglycemia, inflammation of the pancreas, low red and white blood cell count, rashes,

osteoporosis, painful nerve damage, and even death (HHS, 2014a).

The researchers at UCSF who discovered the CD4+T cell pyroptosis issue mentioned earlier in this brief "have identified an existing anti-inflammatory drug that in laboratory tests blocks the death of these cells—and now are planning a Phase 2 clinical trial to determine if this drug or a similar drug can prevent HIV-infected people from developing AIDS and related conditions" (UCSF, 2013).

One focus of HIV/AIDS research is the development of a vaccine to prevent the spread of the HIV virus but results thus far have been disappointing. NIAID recently reported the suspension of the clinical trials of a vaccine because "the investigational vaccine regimen neither prevented HIV infection nor reduced viral load among vaccine recipients who later became infected with the virus" (NIAID, 2013).

In February 2014 researchers announced that another mechanism to discourage HIV from binding to cells has been identified. If certain proteins (gp120) are manufactured in a particular way (addition of a sulfur atom surrounded by four oxygen atoms to the amino acid), "the resulting product would adopt a more true-to-life structure and more closely mirror the way the immune system sees unbound HIV. This might help generate a more effective HIV vaccine" (NIAID, 2014).

In a review of recent research, Barouch and Picker (2014) discussed "the scientific basis and clinical potential of novel adenovirus and cytomegalovirus vaccine vectors for HIV-1 as two contrasting, but potentially complementary, vector approaches" (p. 765) to vaccine development. Novel adenovirus vectors have been shown to partially protect against acquiring the infection as well as aiding in controlling the virus after infection and cytomegaloviruses have demonstrated the ability to control the virus and potentially rid the body of the virus after infection (Barouch and Picker, 2014).

Although there is no real cure for HIV/AIDS, one man became the exception that proves the rule in 2006. Diagnosed with leukemia that required a stem-cell transplant, his doctor was able to find a stem-cell transplant match which lacked the CCR5 receptor, the primary way most HIV strains infect cells (only approximately 1% of the total population lacks CCR5 receptors). Shortly after the stem-cell transplant, the patient was able to stop HIV treatments and tested negative for the virus, effectively making him the first person cured of HIV (The Foundation for AIDS Research, 2012).

National HIV/AIDS Strategy

"On July 13, 2010, the White House released the National HIV/AIDS Strategy (NHAS). This ambitious plan is the nation's first-ever comprehensive coordinated HIV/AIDS roadmap with clear and measurable targets to be achieved by 2015" (CDC, n.d.). The goals of NHAS are: reducing new HIV infections; increasing access to care and improving health outcomes for people living with HIV; and reducing HIV-related health disparities. Some of the major accomplishments and progress made towards achieving those goals include:

- ➤ In 2012, HHS approved a set of seven common core indicators to monitor HHS-funded prevention, treatment, and care services in an effort to standardize data collection and grantee reporting requirements, thereby reducing burdens and increasing efficiency
- New health plans under the Affordable Care Act must offer HIV screening without cost sharing (effective April 2014) as well as prohibit denial based on pre-existing conditions and lifetime caps on coverage

- Preexposure prophylaxis (PrEP) for the prevention of HIV infection clinical practice guidelines published by CDC in May 2014 (CDC, 2014b). Recommended for:
 - Sexually active adult MSM
 - Adult heterosexually active men and women who are at substantial risk of HIV infection
 - Adult injection drug users
- National Institutes of Health (NIH) redirected \$100 million in 2014 to research new therapies towards a cure
- Waiting list for the AIDS Drug Assistance Program (ADAP) have been nearly eliminated by November 2013 from a high of over 9,000 in 2011
- ➢ In 2014, CDC announced the availability of \$210 million to support up to 100 community-based organizations for a 5-year project that will increase access to HIV testing and prevention in communities that are most heavily affected by HIV and improve outcomes along the HIV care continuum
- In 2014, SAMHSA introduced the Minority
 AIDS Initiative Care Pilot: Integration of HIV
 Medical Care Into Behavioral Health
 Programs, which over four years, will
 integrate a comprehensive set of behavioral
 health and medical care services in
 substance abuse and community mental
 health programs that serve racial and ethnic
 minority populations at high risk for
 behavioral health disorders and HIV

(CDC, n.d.; the White House, 2014a&b)

HIV/AIDS Research Brief March 2015

The following table presents the latest report of the status of Texas in meeting the goals of the National HIV/AIDS Strategy:

Goal/	Nat'l	Texas	State	
Indicators	Goal	Texas	Ranking	
Prevent New HIV Infections				
Increase HIV testing by 4%	44.2	42.4	19 of 51	
Reduce late-stage HIV diagnosis by 25%	19.1	23.9 13 of 5		
Improve Access to HIV Care and	d Healti	h Outco	mes	
Reduce death rate among HIV- diagnosed persons by 10%	21.7	22.2	22 of 51	
Reduce HIV-Related Health Disparities				
Increase HIV testing (ever) among racial/ethnic groups by 4%				
Black/African American	68.8	66.4	22 of 51	
Hispanic/Latino	46.6	38.3	40 of 51	
White		41.0	19 of 51	
Other 40.7		35.4	43 of 51	
Reduce late-stage HIV diagnosis among racial/ethnic groups by 25%				
Black/African American 17.6		18.7	11 of 50	
Hispanic/Latino	21.6	30.8	29 of 51	
White	19.5	22.3	9 of 51	
Other 20.4		23.8	19 of 51	
(CDC, 2014c)				

Regional HIV/AIDS Programs

There are currently at least twenty agencies or clinics that provide services for people with

HIV/AIDS in Bexar County; some of these include the Alamo Area Resource Center, Barrio Family Health Center, BEAT AIDS, Center for Health Care Services, Hope Action Care, and the San Antonio AIDS Foundation. The Department of State Health Services in Bandera and Boerne serve patients in San Antonio's outlying counties. These agencies provide most, if not all, of the following resources and services: health and prevention information, counseling, case management, drug assistance, support groups, mental health services, substance abuse treatment, anonymous HIV/AIDS testing, advocacy services, emergency housing assistance, financial assistance, transportation,

clothing, and nutritional support. The San Antonio AIDS Foundation also has a Special Care Facility and Residential AIDS Hospice License, providing medical services and end-oflife care (DSHS, 2014b).

San Antonio also has a variety of agencies that offer AIDS-related services as a part of their broader purpose and operations. Such organizations include the FFACTS/
Immunosuppression Clinic of the University Health System (2015), City of San Antonio Metropolitan Health District (2014) and Planned Parenthood (San Antonio Area HIV Health Services Planning Council, 2014).

Funding Resources for HIV/AIDS

Funding for state HIV/AIDS programs is provided by the Federal government through the Departments of Health and Human Services and Housing and Urban Development as well as the Centers for Disease Control and Prevention (CDC) (KFF, n.d.). Funding for HIV/AIDS programs in Bexar County is also available through the Texas Department of State Health Services, and the Bexar County Department of Community Resources (DCR) (DCR, n.d.).

The Ryan White CARE Act of 1990, which was reauthorized in 2009 is "the single largest federal program designed specifically for people with HIV in the United States" (KFF, 2013). The act secures and provides emergency funds to eligible metropolitan areas (including Bexar County), state funds, early intervention funds, and women, infant, children, and youth funds for community and state services helping people with HIV/AIDS (KFF, 2013). "Ryan White program funds are payors of last resort" (DCR, n.d.) which requires that all other avenues of payment assistance must be exhausted. The following table displays funds received from Federal funding sources by Texas in fiscal year 2013.

TEXAS HIV/AIDS FEDERAL FUNDING FY 2013					
	Funding Agency	Amount			
HIV/AIDS prevention	Centers for Disease Control and Prevention	\$37,756,708			
Housing Opportunities for Persons with AIDS (HOPWA)	Office of HIV/AIDS Housing	\$19,513,6089			
SAMHSA HIV/ AIDS Funding	Substance Abuse and Mental Health Services Administration	\$7,427,168			
OMH HIV/AIDS Funding	Office of Minority Health	\$149,343			
Ryan White Act	Health Resources & Services Administration	\$144,901,036			
Total		\$209,747,863			
(KFF, n.d.)					

Despite progress made since the epidemic began, HIV continues to infect about 50,000 people each year and the virus remains one of the top ten causes of death in the world (the White House, 2014b; WHO, 2014).

REFERENCES

- Barouch, D. and Picker, L. (2014). Novel vaccine vectors for HIV-1. Nat Rev Microbiol. Nov 2014: 12(11): 765-771. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4237164/
- Bexar County Department of Community Resources (DCR). (n.d.). Community health. Retrieved January 22, 2015, from http://www.bexar.org/cdp/CommunityHealth.html
- Centers for Disease Control and Prevention (CDC). (n.d.). National HIV/AID strategy: Fact sheet. Retrieved January 26, 2015, from http://www.cdc.gov/hiv/pdf/policies_nhas-fact-sheet.pdf
- Centers for Disease Control and Prevention (CDC). (2014a). HIV transmission. Retrieved from
 - http://www.cdc.gov/hiv/basics/transmission.html
- Centers for Disease Control and Prevention (CDC). (2014b). Preexposure prophylaxis for the prevention of HIV infection in the United States: 2014 Clinical practice guideline. Retrieved from http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf
- Centers for Disease Control and Prevention (CDC). (2014c). State HIV prevention progress report, 2014. Retrieved from http://www.cdc.gov/hiv/pdf/policies/StateProgressReport2014.pdf
- Centers for Disease Control and Prevention (CDC). (2015). National center for HIV/AIDS, viral hepatitis, STD, and TB prevention Atlas. Retrieved from http://gis.cdc.gov/GRASP/NCHHSTPAtlas/main.html?s cid=nchhstp-
- City of San Antonio Metropolitan Health District. (2014). STD/HIV Services. Retrieved from http://www.sanantonio.gov/health/STDHIV-Mainpage.html
- The Foundation for AIDS Research. (2012). A cure for HIV/AIDS: Recent breakthroughs and new research frontiers. Retrieved from http://www.amfar.org/articles/on-the-hill/2012/a-cure-for-hiv/aids--recentbreakthroughs-and-new-research-frontiers/
- HIV In Site. (2014). Epidemiology of HIV/AIDS in the United States. Retrieved from http://hivinsite.ucsf.edu/InSite?page=kb-01-03#S1.1X

- Kaiser Family Foundation (KFF). (n.d.). Total federal HIV/AIDS grant funding. Retrieved January 22, 2015, from http://kff.org/hivaids/state-indicator/total-federal-grant-funding/
- Kaiser Family Foundation (KFF). (2013). The Ryan White Program. Retrieved from http://www.kff.org/hivaids/upload/7582-06.pdf
- Kaiser Family Foundation (KFF). (2014a). HIV/AIDS policy fact sheet: The HIV/AIDS epidemic in the United States. Retrieved from http://kaiserfamilyfoundation.files.wordpress.com/2013/03/3029-14.pdf
- Kaiser Family Foundation (KFF). (2014b). HIV/AIDS policy fact sheet: Women and HIV/AIDS in the United States. Retrieved from http://www.kff.org/hivaids/upload/6092-10.pdf
- Kaiser Family Foundation (KFF). (2015a). Percentage of persons aged 18-64 who reported ever receiving an HIV test. Retrieved January $21,\,2015,\,from\,\,\underline{\text{http://kff.org/hivaids/state-indicator/hiv-testing-rate-ever-tested/}}$
- National Institute of Allergy and Infectious Diseases (NIAID). (2009). HIV /AIDS: More on how HIV causes AIDS. Retrieved from $\underline{\text{http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/howHIVCausesAIDS/Pages/howhitesalled} = \underline{\text{http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/howHIVCausesAIDS/Pages/howhitesalled} = \underline{\text{http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/howhitesalled} = \underline{\text{http://www.niaid.nih.gov/topics/H$
- National Institute of Allergy and Infectious Diseases (NIAID). (2013). Vaccine regimen study. Retrieved from http://www.niaid.nih.gov/news/QA/Pages/HVTN505qa2013.aspx
- National Institute of Allergy and Infectious Diseases (NIAID). (2014). NIH scientists find mechanism that helps HIV evade antibodies, stabilize key proteins. Retrieved from http://www.niaid.nih.gov/news/newsreleases/2014/Pages/gp120sulfation.aspx
- San Antonio Area HIV Health Services Planning Council. (2014). Testing providers. Retrieved from http://www.hiv210.org/index.php?option=com_content&view=article&id=21&Itemid=1
- Texas Department of State Health Services (DSHS.) (2014a). 2012 Texas HIV program annual report. Retrieved from http://www.dshs.state.tx.us/hivstd/info/annual.shtm
- Texas Department of State Health Services (DSHS). (2014b). HIV/STD service providers. Retrieved from http://www.dshs.state.tx.us/hivstd/services/service s.shtm#sanantonio
- Texas Department of State Health Services (DSHS.) (2014c). Texas HIV surveillance report 2013. Retrieved from http://www.dshs.state.tx.us/hivstd/reports/default.shtm
- University Heath System. (2015). FFACTS family focused AIDS clinical treatment services. Retrieved from http://www.universityhealthsystem.com/about-ffacts
- University of California San Francisco. (December, 2013). Scientists discover how key immune cells die during HIV infection and identify potential drug to block AIDS. Retrieved from http://www.ucsf.edu/news/2013/12/110841/scientists-discover-how-key-immunecells-die-during-hiv-infection-and-identify
- U.S. Census. (2015). Annual estimates of the resident population by sex, race alone or in combination, and Hispanic origin for the United States, States, and Counties: April 1, 2010 to July 1, 2012: 2012 population estimates: table PEPSR5H. Retrieved from $\underline{\text{http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=bkmker.pdf} \\$
- U.S. Department of Health and Human Services: AIDSinfo (HHS). (2014). HIV overview. Retrieved from http://aidsinfo.nih.gov/education-materials/fact-sheets/21/58/fda-
- The White House. (2014a). Fact Sheet: Progress in four years of the national HIV/AIDS strategy. Retrieved from https://blog.aids.gov/2014/07/fact-sheetrogress-in-four-years-of-the-national-hivaids-strategy.html
- The White House. (2014b). National HIV/AIDS strategy: Update of 2014 federal actions to achieve national goals and improve outcomes along the HIV care continuum. Retrieved from
- World Health Organization (WHO). (2014). The top 10 causes of death. Retrieved from http://www.who.int/mediacentre/factsheets/fs310/en/