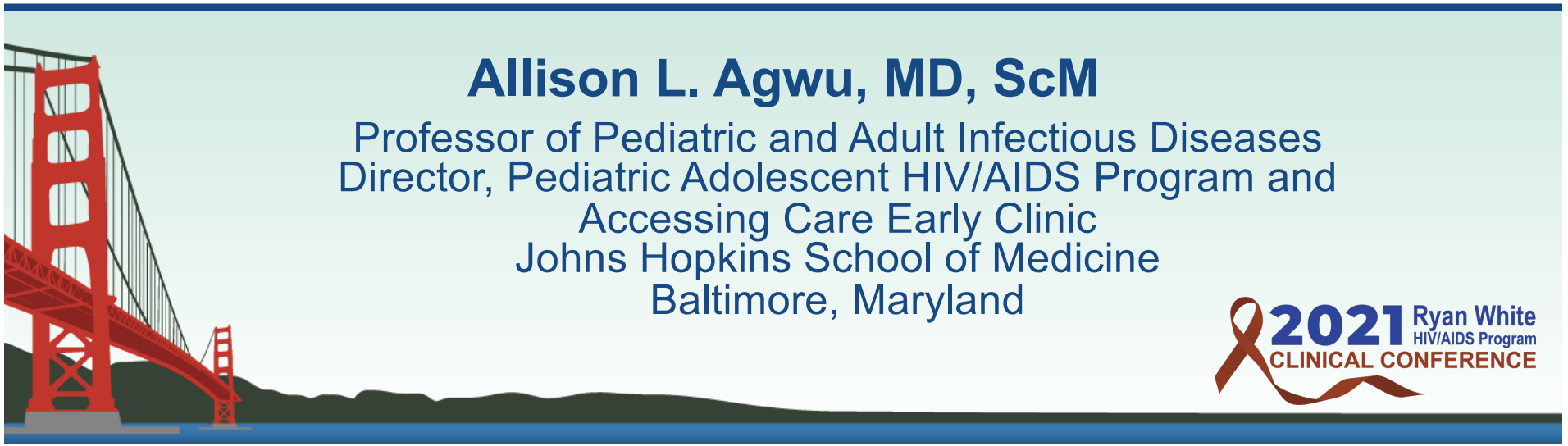
Preventing HIV-Related Comorbidities in Adolescents



Allison L. Agwu, MD, ScM

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Agwu has served on the scientific advisory boards for Gilead Sciences, Inc., and Merck & Co, Inc. (Updated 9/29/21)

Learning Objectives

At the end of this presentations, learners will be able to:

- Review the epidemiology of adolescents living with HIV
- Describe risk factors for developing comorbidities over the life course among adolescents with HIV
- Discuss opportunities to prevent comorbidities and optimize outcomes

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PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

"although they make up only 1% of AIDS patients, they have unique clinical, social, and public health problems that require special attention." Rogers

Acquired Immunodeficiency Syndrome in Children: Report of the Center Control National Surveillance, 1982 to 1985
Martha F. Rogers, Pauline A. Thomas, E. Thomas Starcher, Mary C. Noa, Timothy J. Bush and Harold W. Jaffe

First known infant to be born with HIV

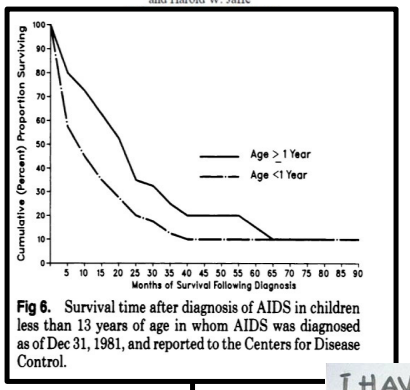
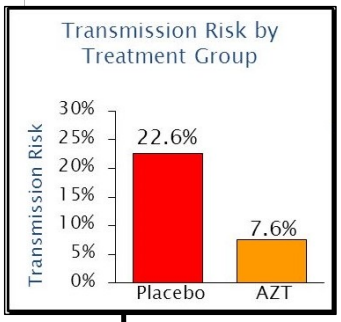
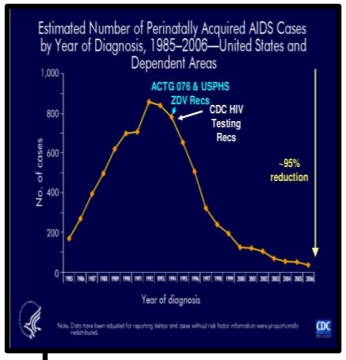
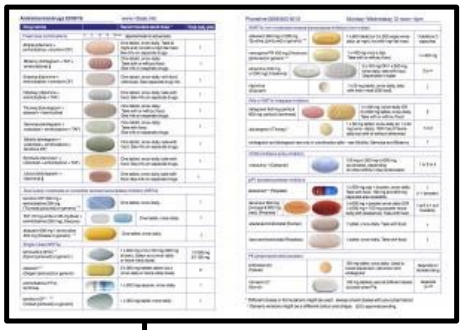
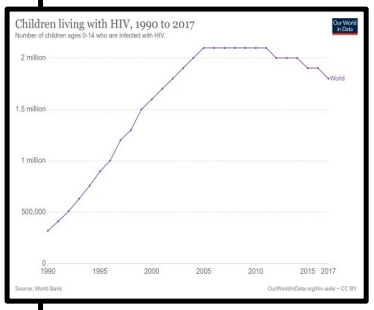


Fig 6. Survival time after diagnosis of AIDS in children less than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1981, and reported to the Centers for Disease Control.









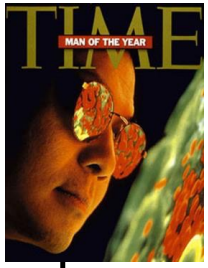
RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men in New York and California —8 Died Inside 2 Years

By LAWRENCE K. ALTMAN.

Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer. Eight of the victims died less than 24 months after the diagnosis was made.

The cause of the outbreak is unknown, and there is as yet no evidence of contagion. But the doctors who have made the



FDA approves 1st HIV ab test

FDA approves Nelfinavir for kids

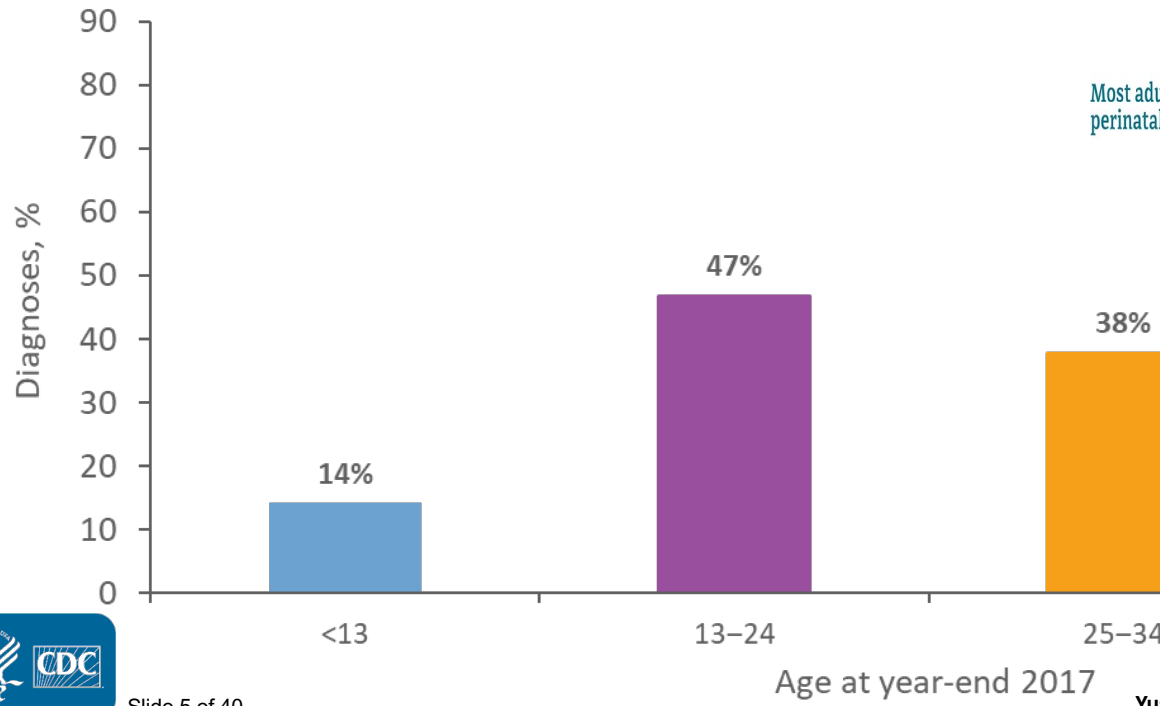
'Cured' HIV Baby is Infected, Doctors Find

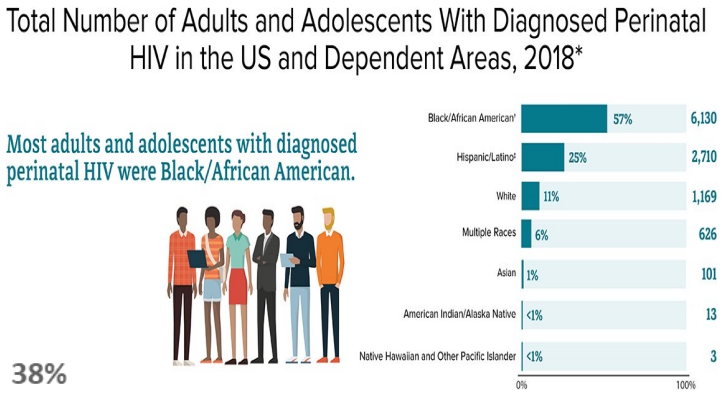
South African child in HIV remission without drugs

1977 1980 1982 1985 1987 1988 1990 1994 1996 2003 2006 2013 2014 2015 2017 2020 2021

https://www.hiv.gov/sites/default/files/aidsgov-timeline.pdf; Rogers et al. 1987 (79): 1008-1014

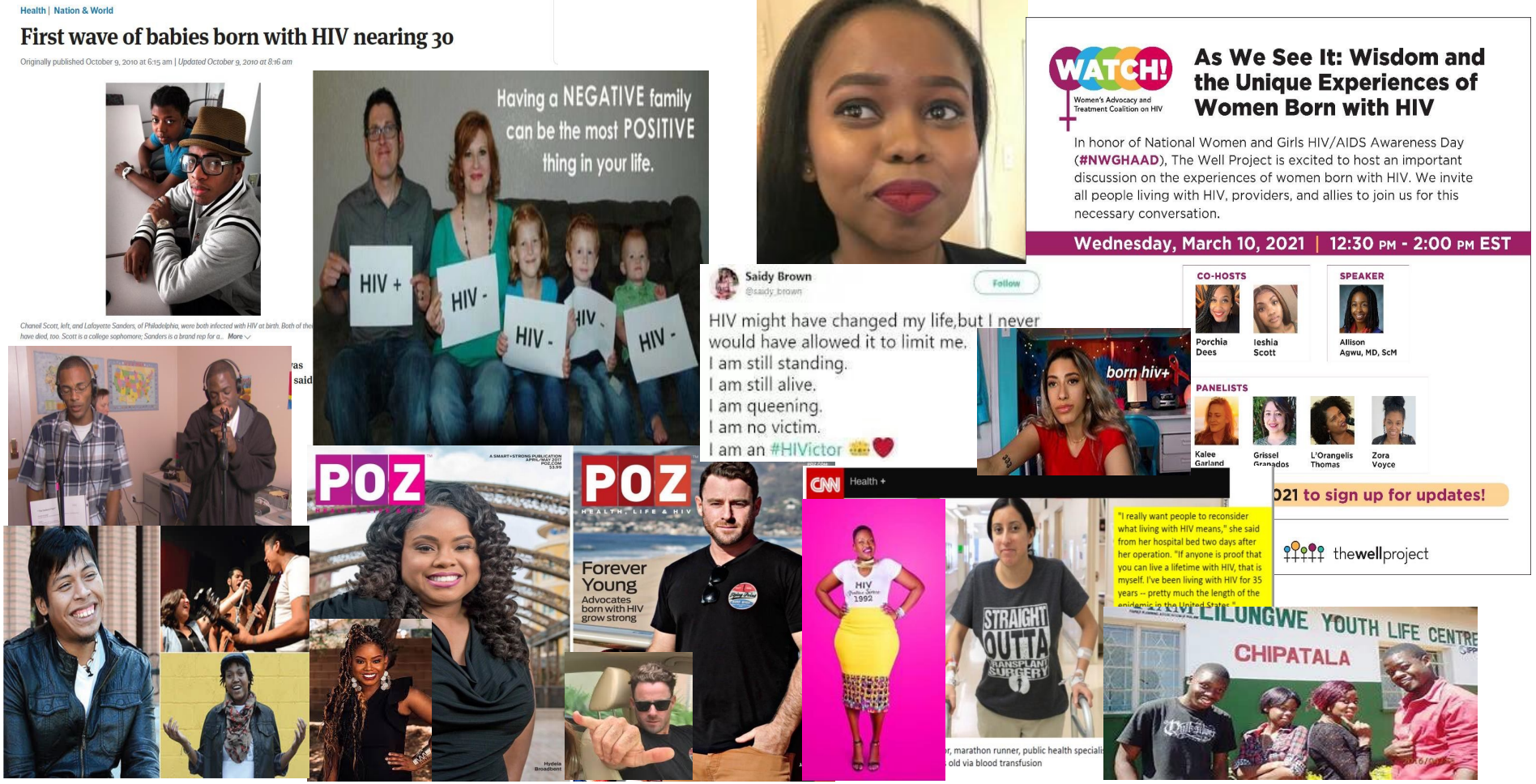
Age Distribution of Persons Living with Diagnosed Perinatally Acquired HIV Infection, Year-end 2017—United States and 6 Dependent Areas (N = 11,924)





Yusuf and Agwu. Expert Review of Anti-Infective Therapy. Sep 2020

Many AYA born with HIV are thriving……



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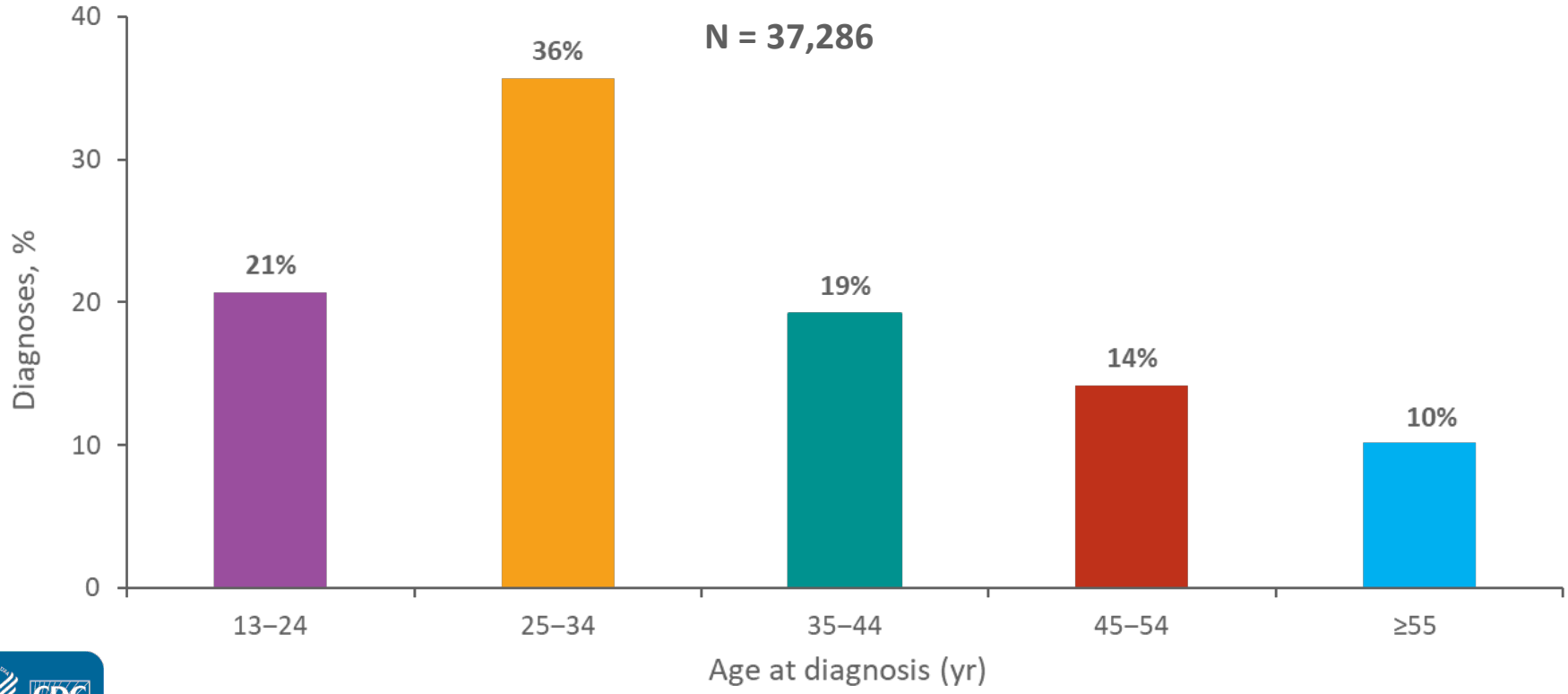
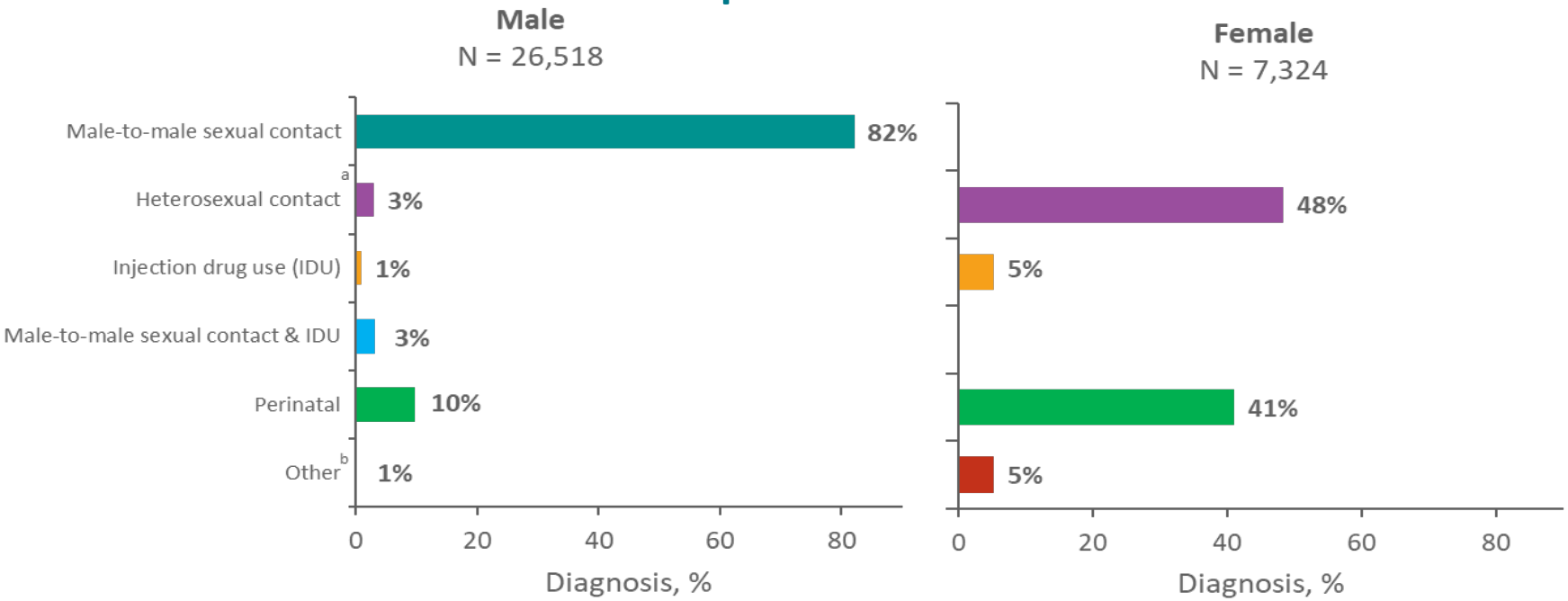
Diagnoses of HIV Infection among Adults and Adolescents by Age at Diagnosis, 2018—United States



Note. Data for the year 2018 are considered preliminary and based on 6 months reporting delay.

Adolescents and Young Adults Aged 13–24 Years Living with Diagnosed HIV Infection by Sex and Transmission Category, Year-end 2017—United States and 6 Dependent Areas



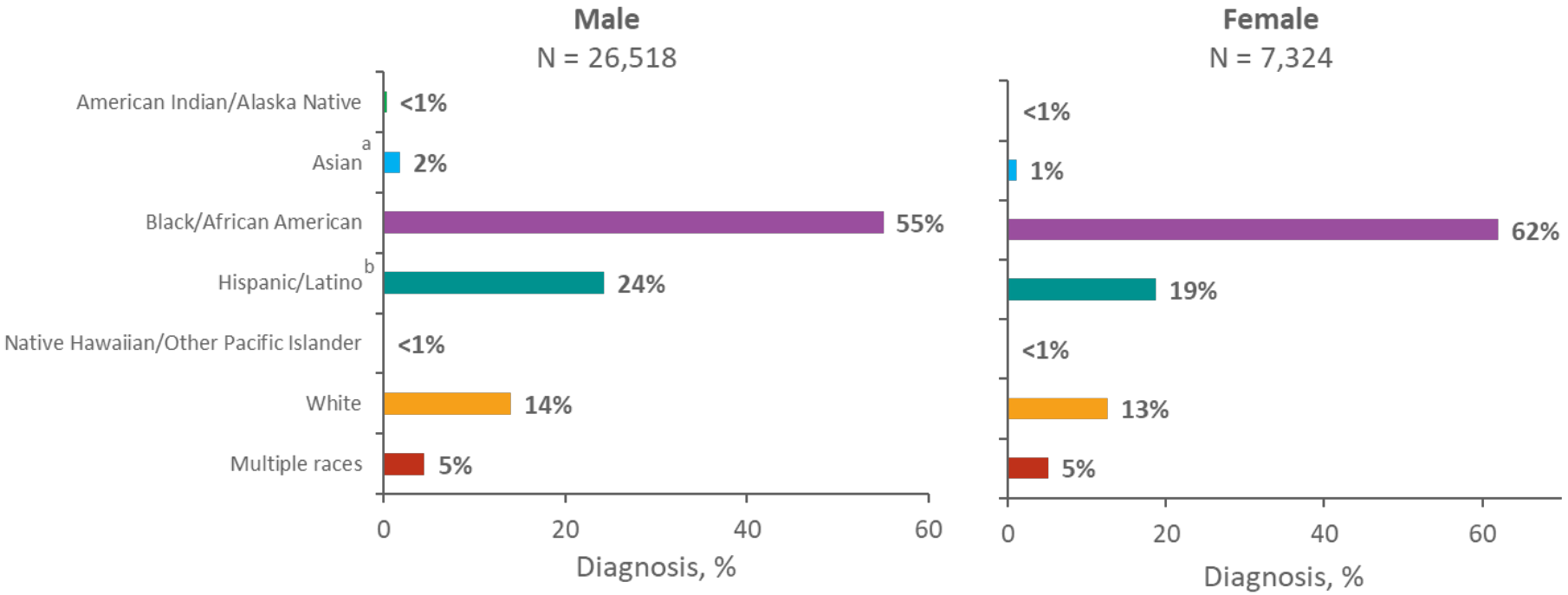
Note. Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises 1% or less of cases.

[a] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

[b] Includes hemophilia, blood transfusion, and risk factor not reported or not identified.

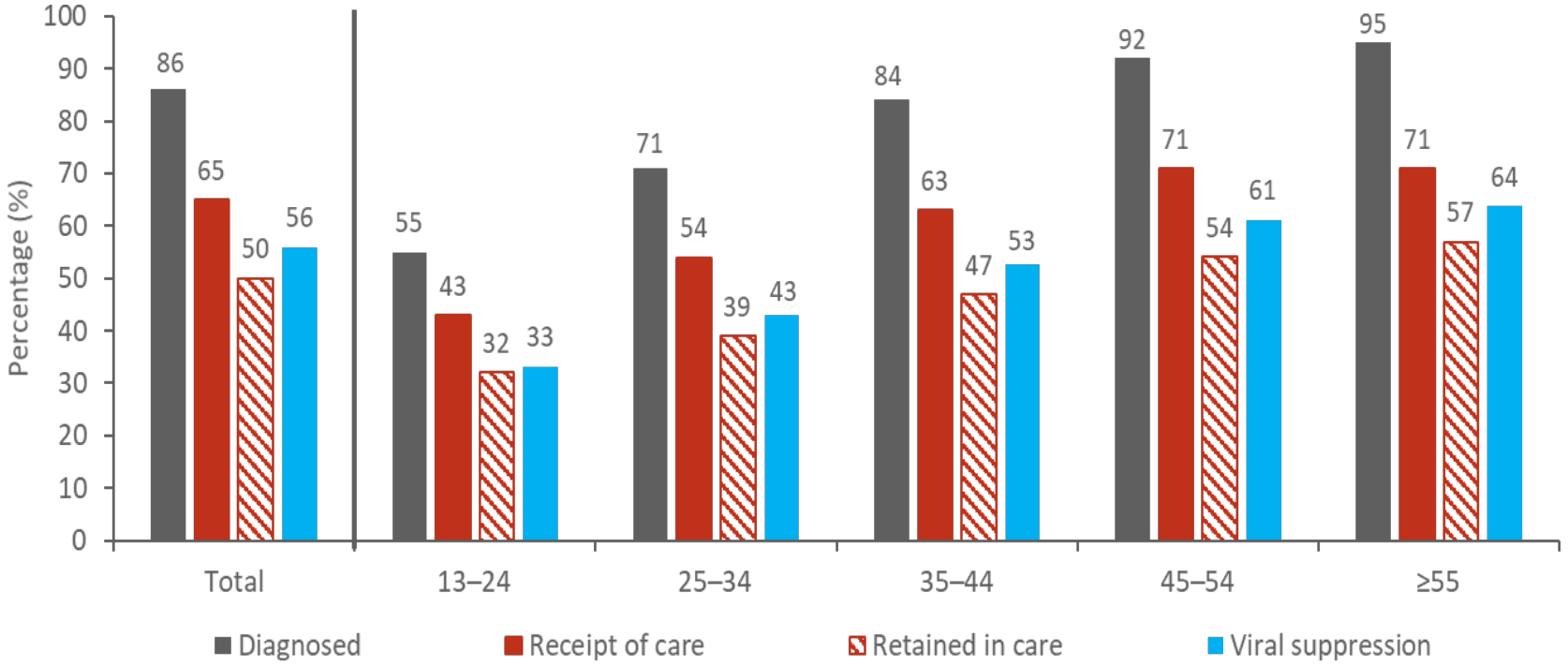
Yusuf & Agwu. Expert Review of Anti-Infective Therapy. Sep 2020

Adolescents and Young Adults Aged 13–24 Years Living with Diagnosed HIV Infection, by Sex and Race/Ethnicity, Year-end 2017—United States and 6 Dependent Areas



[a] Includes Asian/Pacific Islander legacy cases.
[b] Hispanics/Latinos can be of any race.

Persons Living with Diagnosed or Undiagnosed HIV Infection
HIV Care Continuum Outcomes, by Age, 2018—United States



Note. Receipt of medical care was defined as ≥1 test (CD4 or VL) in 2018. Retained in continuous medical care was defined as ≥2 tests (CD4 or VL) ≥3 months apart in 2018. Viral suppression was defined as <200 copies/mL on the most recent VL test in 2018.


I>AV
I>AV
I>AV
I>AV
I>AV
I am greater than my highs and lows.
I>AV
type one
I>AV

Life course perspective for adolescents with HIV

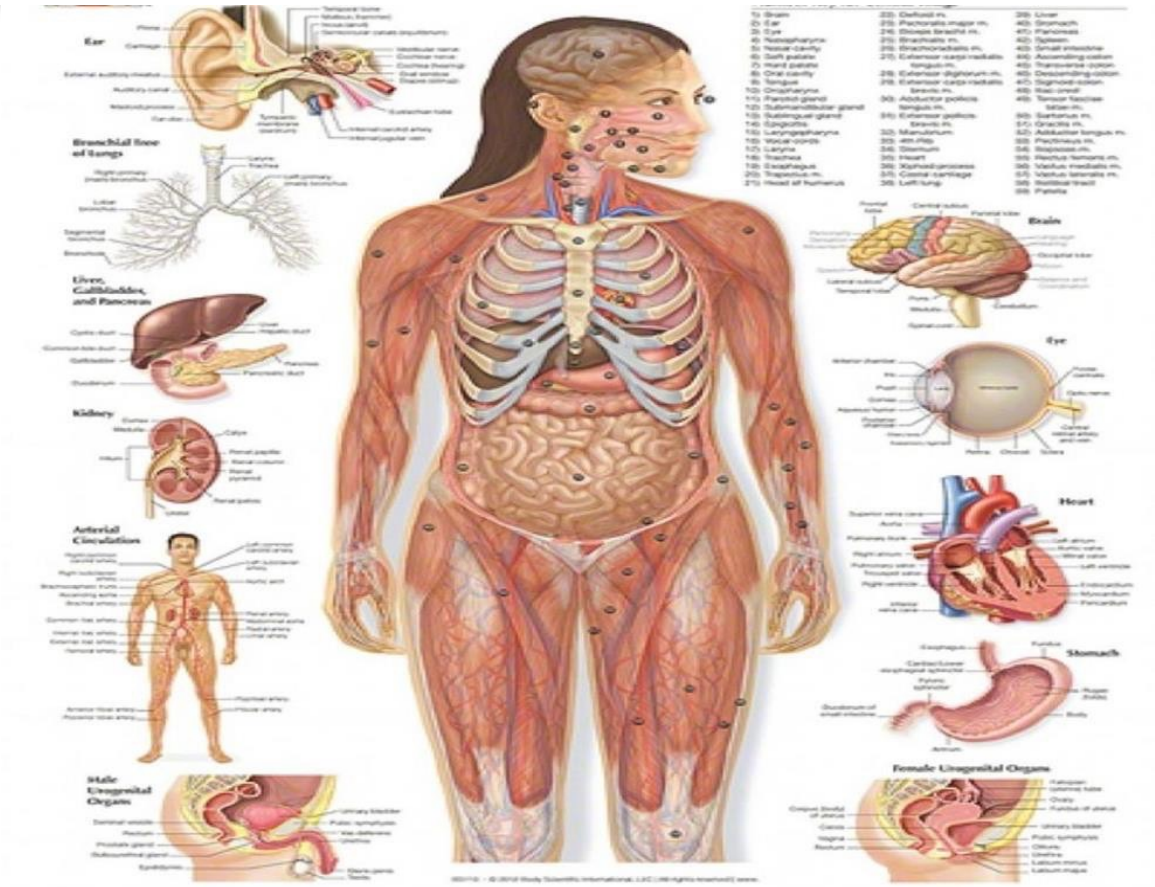
	2nd Decade 10-19 years
	
Life events	School Trade School/College Employment Parent/guardian loss
Self-management	Parental/caregiver involvement wanes
Disclosure	Disclosure (to self) Disclosure to others
Stigma	Internal and external stigma

Zinyemba TP et al. J Econ Surveys 2019; **Yusuf** and Agwu. Expert Review of Anti-Infective Therapy. Sep 2020

Life course perspective for adolescents with HIV

	2nd Decade 10-19 years	3rd Decade 20-29 years	4th Decade 30-39 years	5th Decade 40-49 years	≥6th Decade ≥50 years
					
Treatment and Treatment-related Factors					
Antiretroviral treatment	Simple regimens* Increased responsibility of ART	Simple regimen Increased complex regimens due to development of resistance Full responsiblilty of ART	Simple regimen Increased complex regimens due to development of resistance Full responsiblilty of ART		

Yusuf and Agwu 2021



How will adolescents with HIV infection be impacted?

Deeks SG 2013; Vance DE et al. Am J Nurs. 2010 March ; 110(3): 42–49.

Leading Cause of Death in the United States for Select Age Groups (2019)
Data Courtesy of CDC

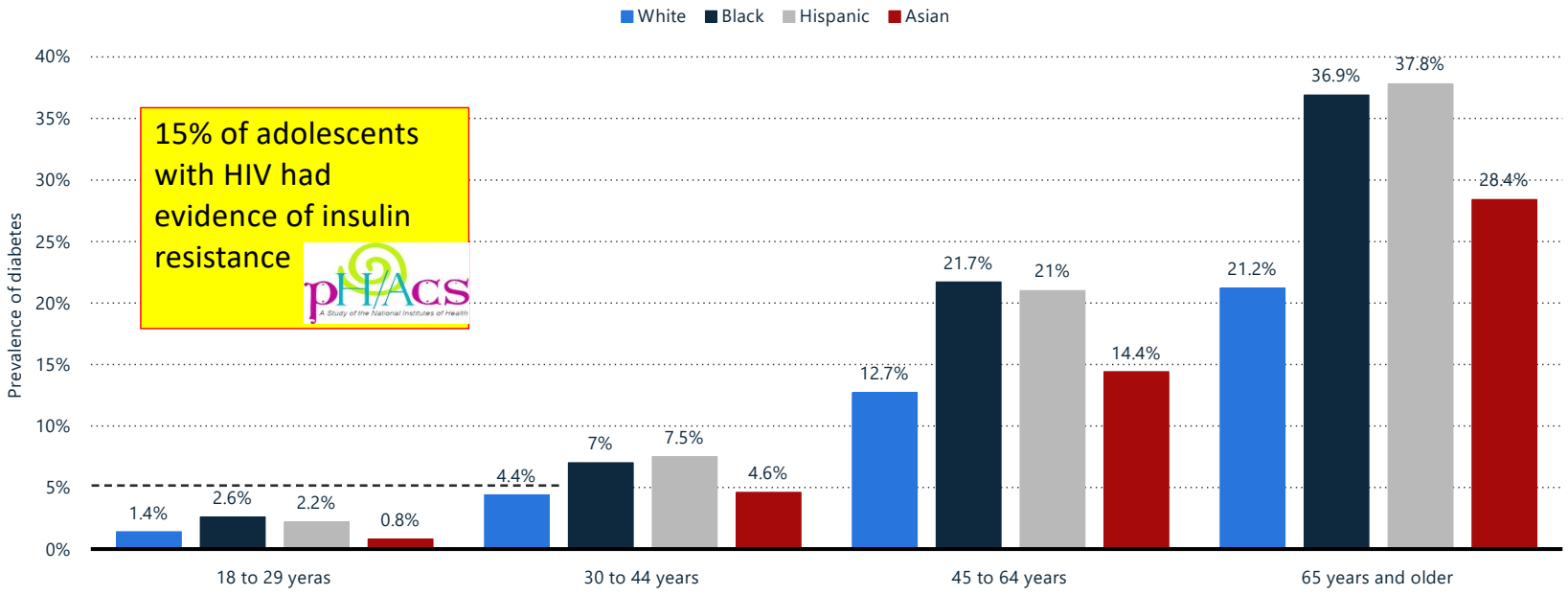
Rank	10-14	15-24	25-34	35-44	45-54	55-64	All Ages
1	Unintentional Injury 778	Unintentional Injury 11,755	Unintentional Injury 24,516	Unintentional Injury 24,070	Malignant Neoplasms 35,587	Malignant Neoplasms 111,765	Heart Disease 659,041
2	**Suicide 534**	**Suicide 5,954**	**Suicide 8,059**	Malignant Neoplasms 10,695	Heart Disease 31,138	Heart Disease 80,837	Malignant Neoplasms 599,601
3	Malignant Neoplasms 404	Homicide 4,774	Homicide 5,341	Heart Disease 10,499	Unintentional Injury 23,359	Unintentional Injury 24,892	Unintentional Injury 173,040
4	Homicide 191	Malignant Neoplasms 1,388	Malignant Neoplasms 3,577	**Suicide 7,525**	Liver Disease 8,098	CLRD 18,743	CLRD 156,979
5	Congenital Anomalies 189	Heart Disease 872	Heart Disease 3,495	Homicide 3,446	**Suicide 8,012**	Diabetes Mellitus 15,508	Cerebro-vascular 150,005
6	Heart Disease 87	Congenital Anomalies 390	Liver Disease 1,112	Liver Disease 3,417	Diabetes Mellitus 6,348	Liver Disease 14,385	Alzheimer's Disease 121,499
7	CLRD 81	Diabetes Mellitus 248	Diabetes Mellitus 887	Diabetes Mellitus 2,228	Cerebro-vascular 5,153	Cerebro-vascular 12,931	Diabetes Mellitus 87,647
8	Influenza & Pneumonia 71	Influenza & Pneumonia 175	Cerebro-vascular 585	Cerebro-vascular 1,741	CLRD 3,592	**Suicide 8,238**	Nephritis 51,565
9	Cerebro-vascular 48	CLRD 168	Complicated Pregnancy 532	Influenza & Pneumonia 951	Nephritis 2,269	Nephritis 5,857	Influenza & Pneumonia 49,783
10	Benign Neoplasms 35	Cerebro-vascular 158	HIV 486	Septicemia 812	Septicemia 2,176	Septicemia 5,672	**Suicide 47,511**

CLRD: Chronic Lower Respiratory Disease

Note: Suicide is not among the ten leading causes of death among children in the 0-9 year age group nor in adults in the age group 65 years and older.

CDC

Percentage of adults in the U.S. with diabetes as of 2016, by age and ethnicity

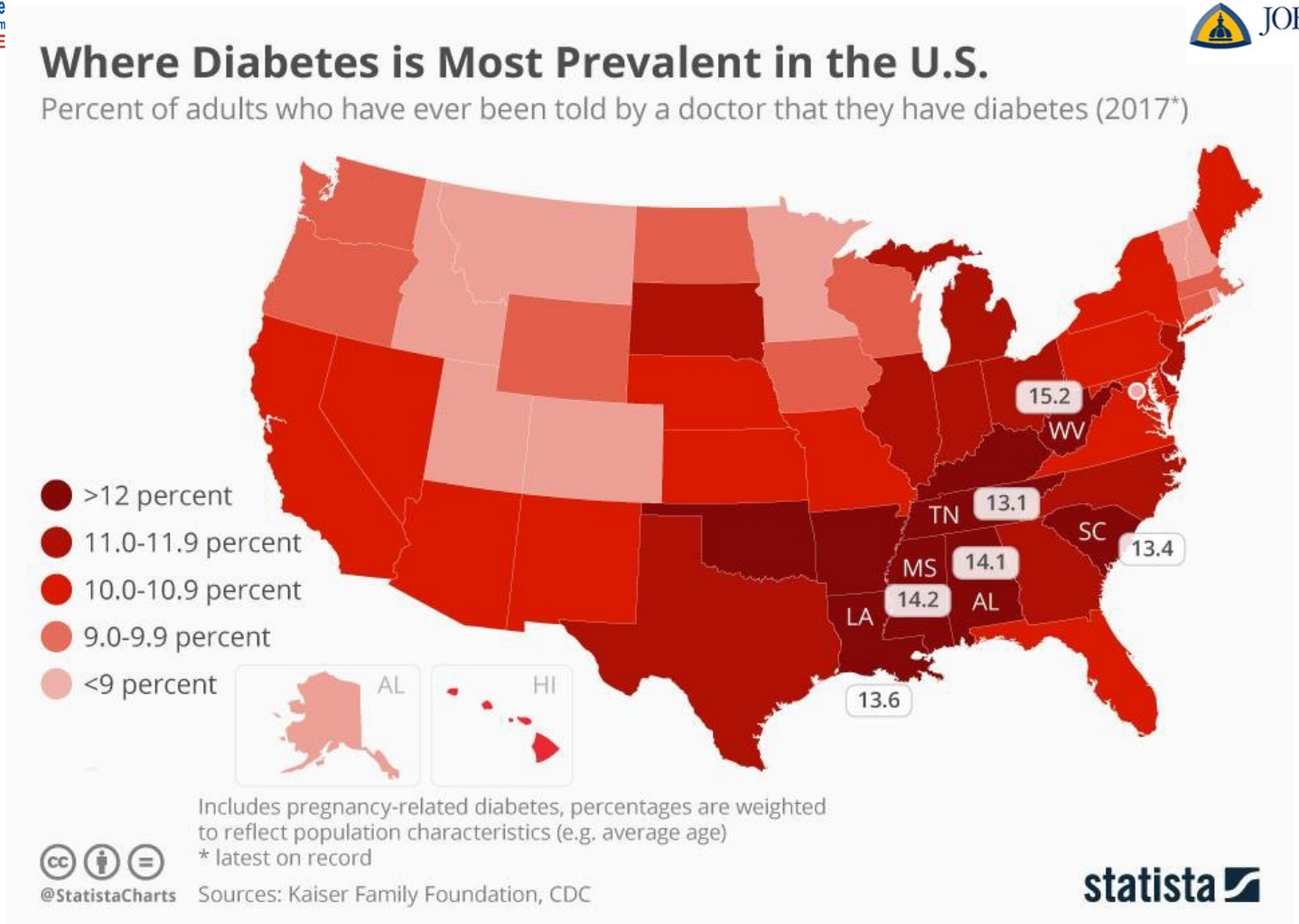


2

Note(s): United States; January 2 to December 30, 2016; 18 years and older; 177,192 respondents; Full or part time workers
Further information regarding this statistic can be found on page 8.
Source(s): Gallup (Gallup-Sharecare Well-Being Index); Sharecare; ID 790778

statista

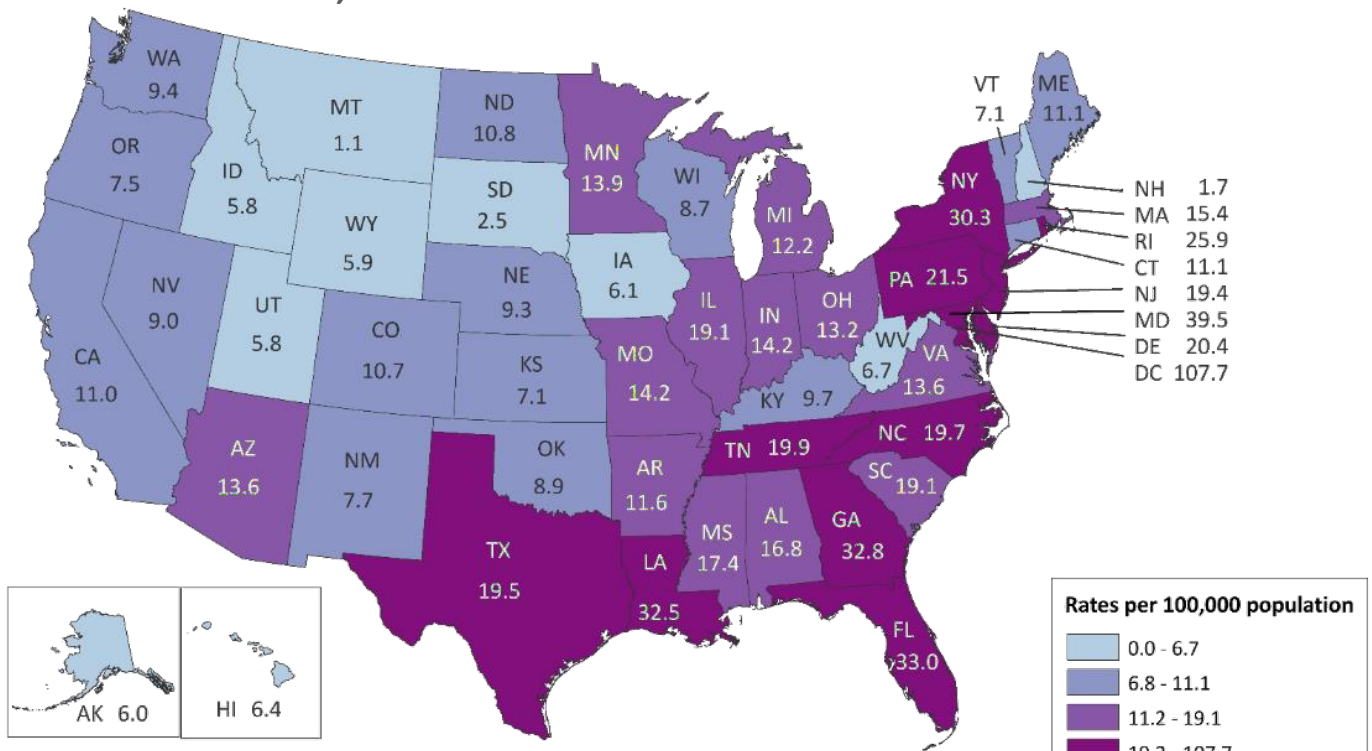
Geffner ME. Horm Res Paediatr 2011; 76: 386-91


Where Diabetes is Most Prevalent in the U.S.
Percent of adults who have ever been told by a doctor that they have diabetes (2017*)
>12 percent
11.0-11.9 percent
10.0-10.9 percent
9.0-9.9 percent
<9 percent
15.2
WV
13.1
TN
SC
13.4
MS
14.1
14.2
AL
LA
13.6
AL
HI
Includes pregnancy-related diabetes, percentages are weighted to reflect population characteristics (e.g. average age)
* latest on record
@StatistaCharts
Sources: Kaiser Family Foundation, CDC
statista

Rates of Adolescents Aged 13–19 Years Living with Diagnosed HIV Infection

Year-end 2017—United States and 6 Dependent Areas

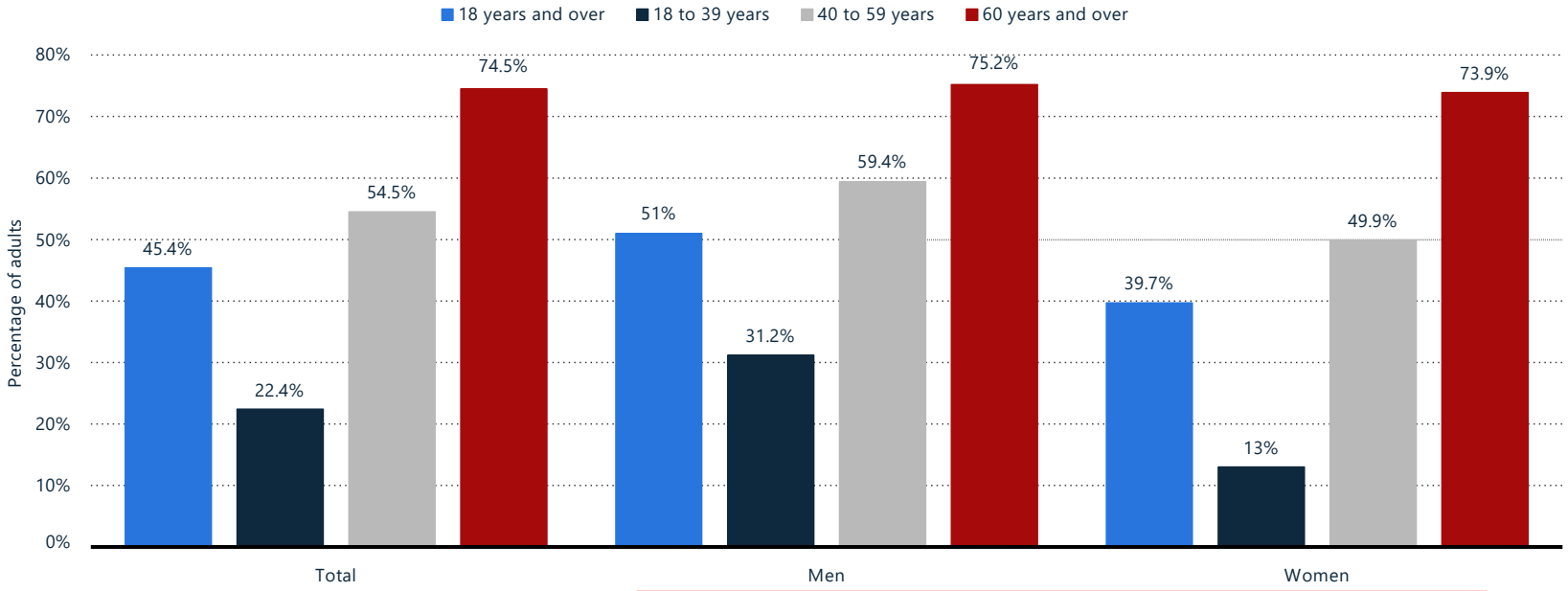
N = 5,222 **Total Rate = 17.6**



American Samoa	0.0
Guam	5.0
Northern Mariana Islands	0.0
Puerto Rico	14.6
Republic of Palau	0.0
U.S. Virgin Islands	34.3

Note. Data are based on address of residence as of December 31, 2017 (i.e., most recent known address).

Prevalence of hypertension among adults in the U.S. in 2017 and 2018, by age and gender



2

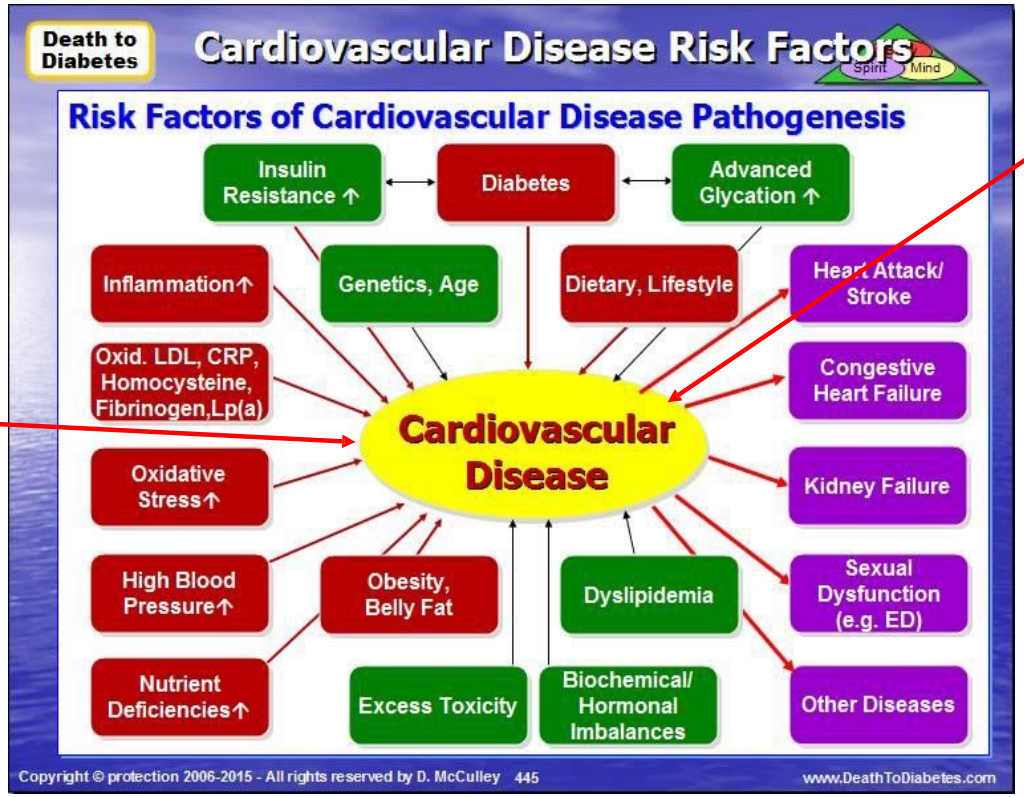
Note(s): United States; 2017 and 2018; 18 years and older
Further information regarding this statistic can be found on page 8.
Source(s): NCHS (National Health and Nutrition Examination Survey); CDC; ID 778065

Adolescent boys (15-19%); adolescent girls (7-12%)
Flynn JT et al. Pediatrics 2017
Among HIV+ youth ??20% (confounded) Sainz et al PIDJ 2016

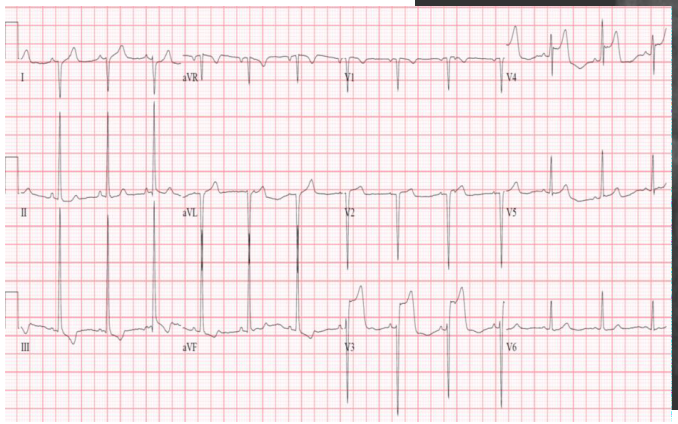
statista

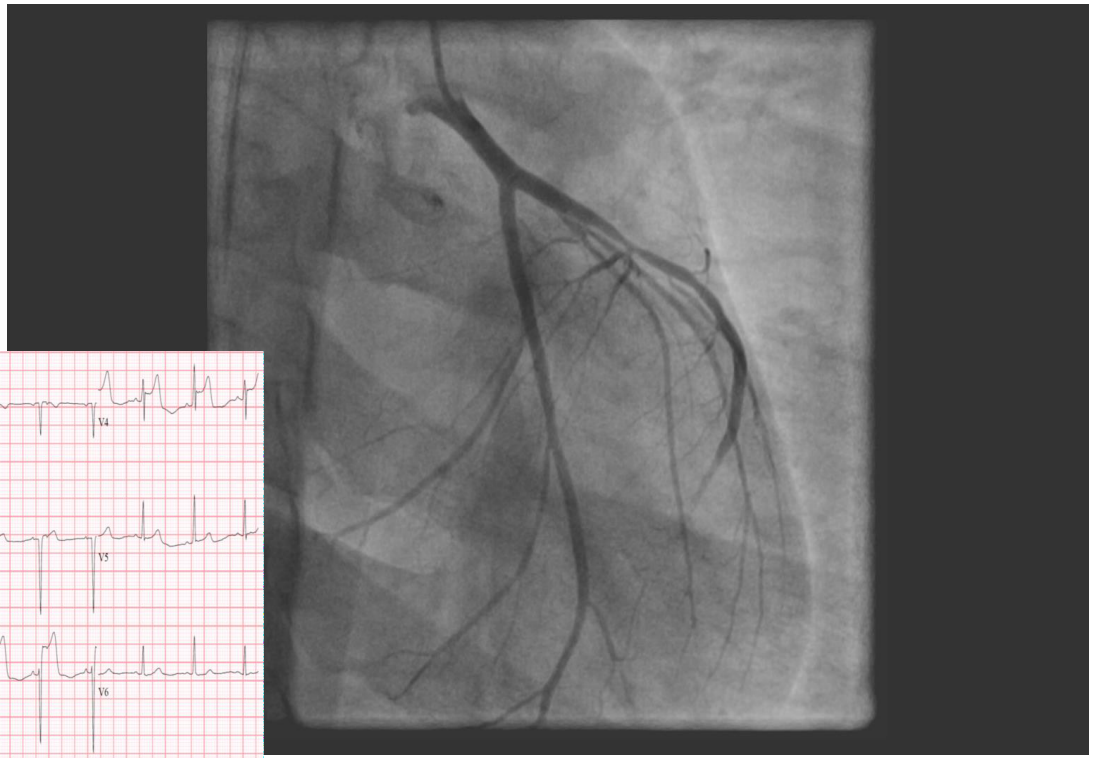
ART?

HIV


Death to Diabetes
Cardiovascular Disease Risk Factors
Spirit
Mind
Risk Factors of Cardiovascular Disease Pathogenesis
Insulin Resistance ↑
Diabetes
Advanced Glycation ↑
Inflammation↑
Genetics, Age
Dietary, Lifestyle
Heart Attack/ Stroke
Oxid. LDL, CRP, Homocysteine, Fibrinogen,Lp(a)
Congestive Heart Failure
Cardiovascular Disease
Oxidative Stress↑
Kidney Failure
High Blood Pressure↑
Obesity, Belly Fat
Dyslipidemia
Sexual Dysfunction (e.g. ED)
Nutrient Deficiencies↑
Excess Toxicity
Biochemical/ Hormonal Imbalances
Other Diseases
Copyright © protection 2006-2015 - All rights reserved by D. McCulley 445
www.DeathToDiabetes.com

23 year old with HIV and acute chest pain



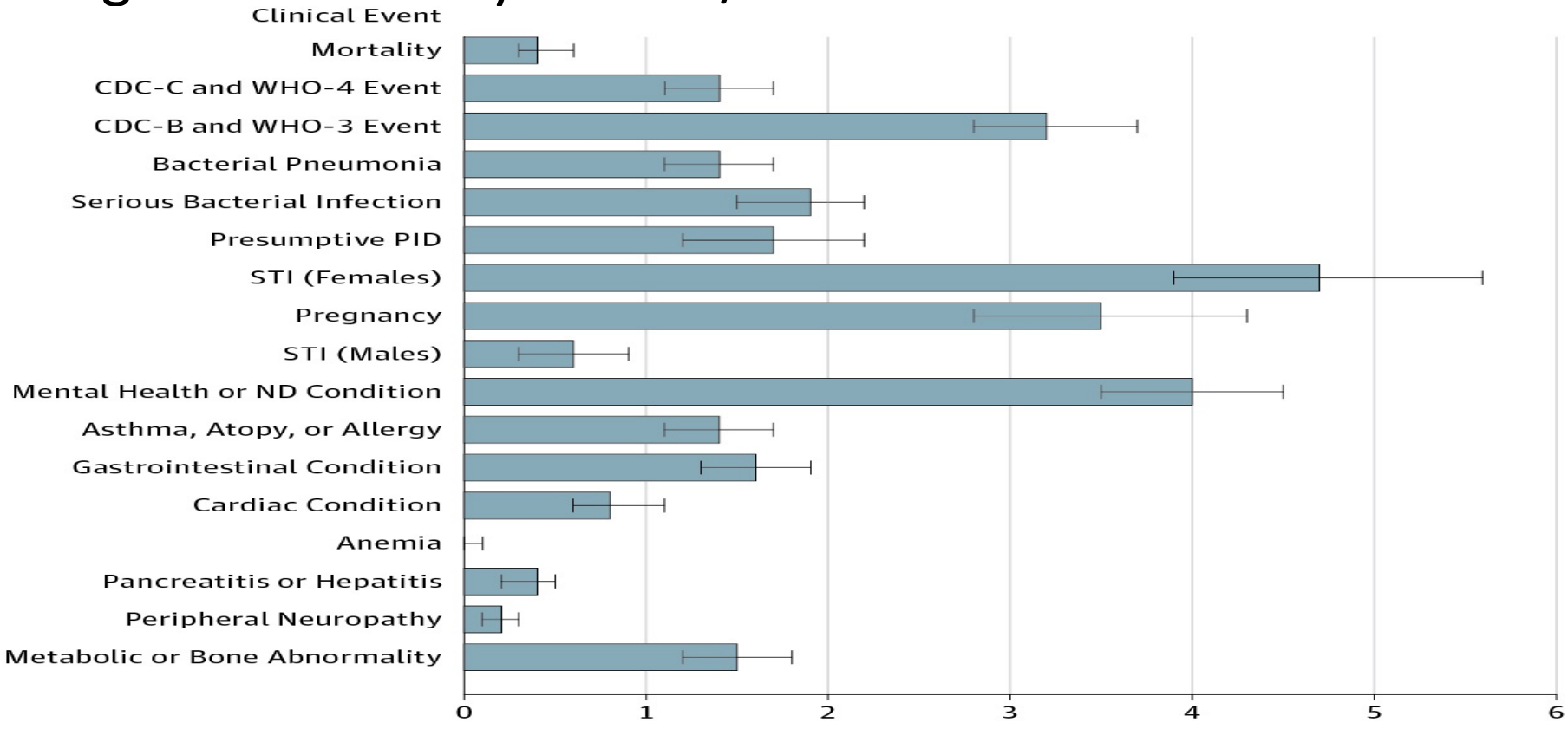


CVD Data for Youth with HIV

- **Studies of children and youths in non-HIV disease states (diabetes, obesity) link arterial stiffness and thickness to hypertension & increased left ventricular mass**
- **Limited data on youth with perinatal infection**
  - ↑ arterial thickness (carotid intimal medial thickness) in HIV+ vs. HIV-
  - ↑ arterial stiffness (pulse wave velocity) & ↓ flow-mediated dilatation in HIV+ vs. HIV-
  - ↑ inflammatory markers in HIV+ vs. HIV- ➔ associated with arterial thickness, stiffness, and flow-mediated dilatation
  - ↑ inflammatory markers despite longstanding virologic suppression
  - AYA with HIV have higher markers of cardiopulmonary dysfunction
    - Up to 28% show evidence of early cardiovascular dysfunction
    - Biomarkers of cardiomyocyte stress and injury (high sensitivity cardiac troponin-T [hs-cTnT] and N-terminal-pro-brain natriuretic peptide [NT- proBNP]) are elevated compared to uninfected adolescents after adjusting for adherence to ART,
    - Inflammation associated with poorer left ventricular function and increased stress in the ventricular walls

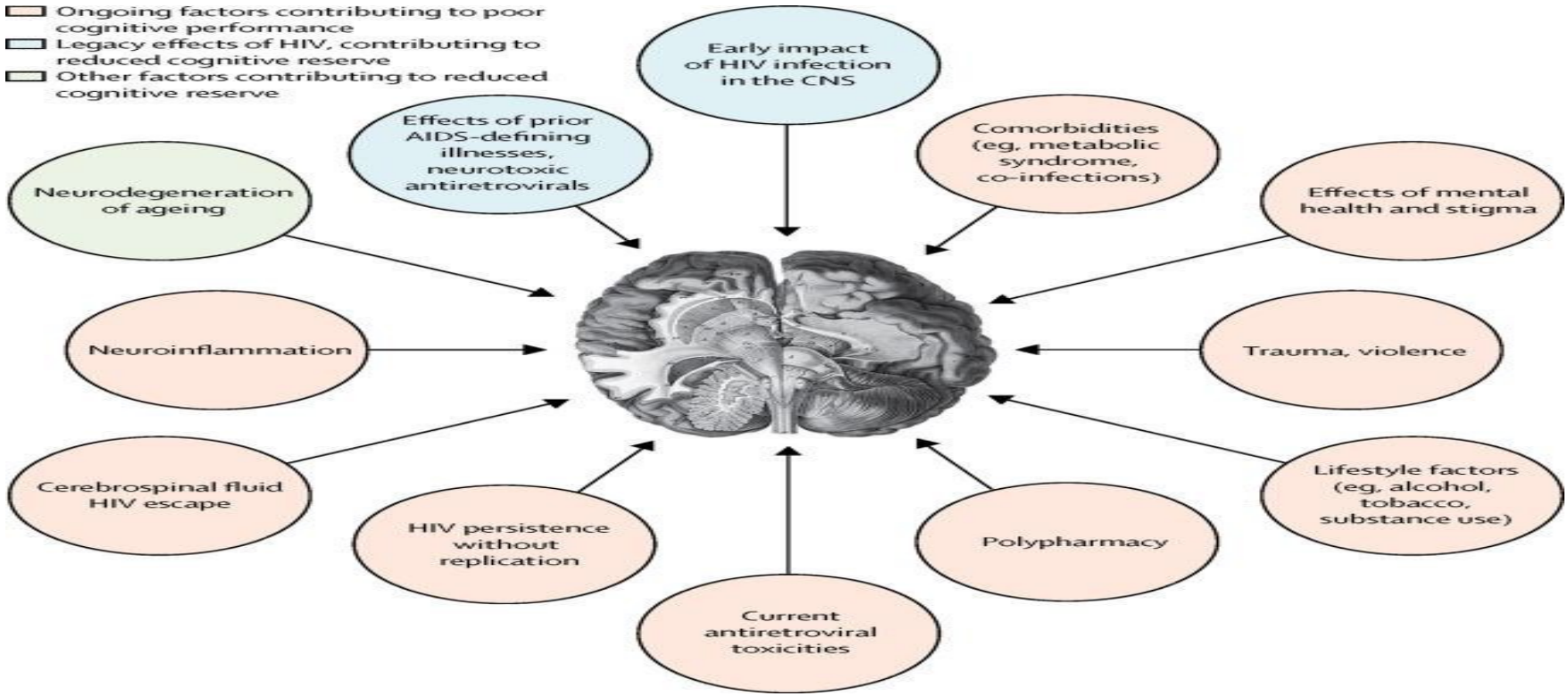
Miller TI, et al. HIV Med. 2012 13(5): 264-75; Sainz T et al Atherosclerosis 2014, Ross et al, Persaud D JAMA Peds 2014, Yusuf 2020

Long-term morbidity of HIV +/- ART



Griffith D et al. OFID 2017; Hazra R et al.; Izbudak, Agwu J Neurorad 2013;, **Venkataramani** 2012; Eckard et al Curr HIV/AIDS 2016; **Neilan** et al JAMA Peds 2017

Mental health in adults born with HIV



Phillips Pediatrics 2016; Malee AIDS Care 2011; Scharko AIDS Care 2006; Earnshaw AIDS & Behavior 2018; Well Project; Winston A et al Lancet HIV 2020

Sexual and reproductive health for adults born with HIV

	2nd Decade 10-19 years	3rd Decade 20-29 years	4th Decade 30-39 years	5th Decade 40-49 years	≥6th Decade ≥50 years
					
Sexual and Reproductive Health					
Sex/reproductive	Sexual and gender identify evolving; Sexual activity often commences Risk reduction	Secondary Prevention Child bearing Risk reduction	Secondary Prevention Child bearing Risk reduction	Secondary Prevention Risk reduction	

Phillips Pediatrics 2016; Malee AIDS Care 2011; Scharko AIDS Care 2006; Earnshaw AIDS & Behavior 2018; Yusuf 2020

STI Rates among adolescents

Rates of chlamydia, gonorrhea, and primary & secondary syphilis ↑ for both sexes in 15–24 year olds (2013-2017)

Chlamydia: highest among women; males ↑ 29%, females ↑ 9%

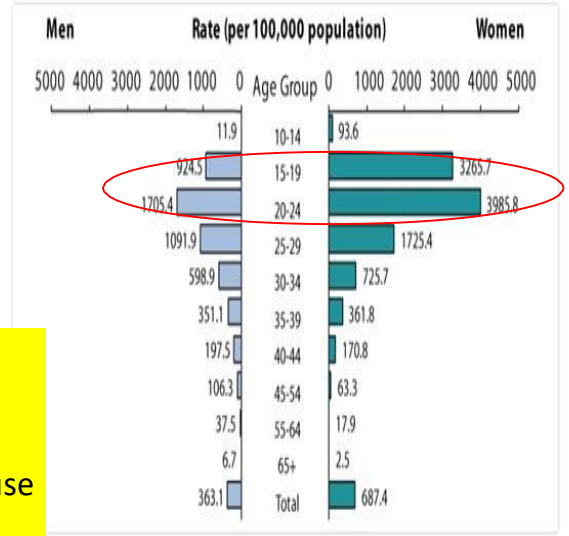
Gonorrhea: males ↑ 52%, females ↑ 24%

Reasons include: incidence, screening , extragenital screening

HIV positive adolescents:

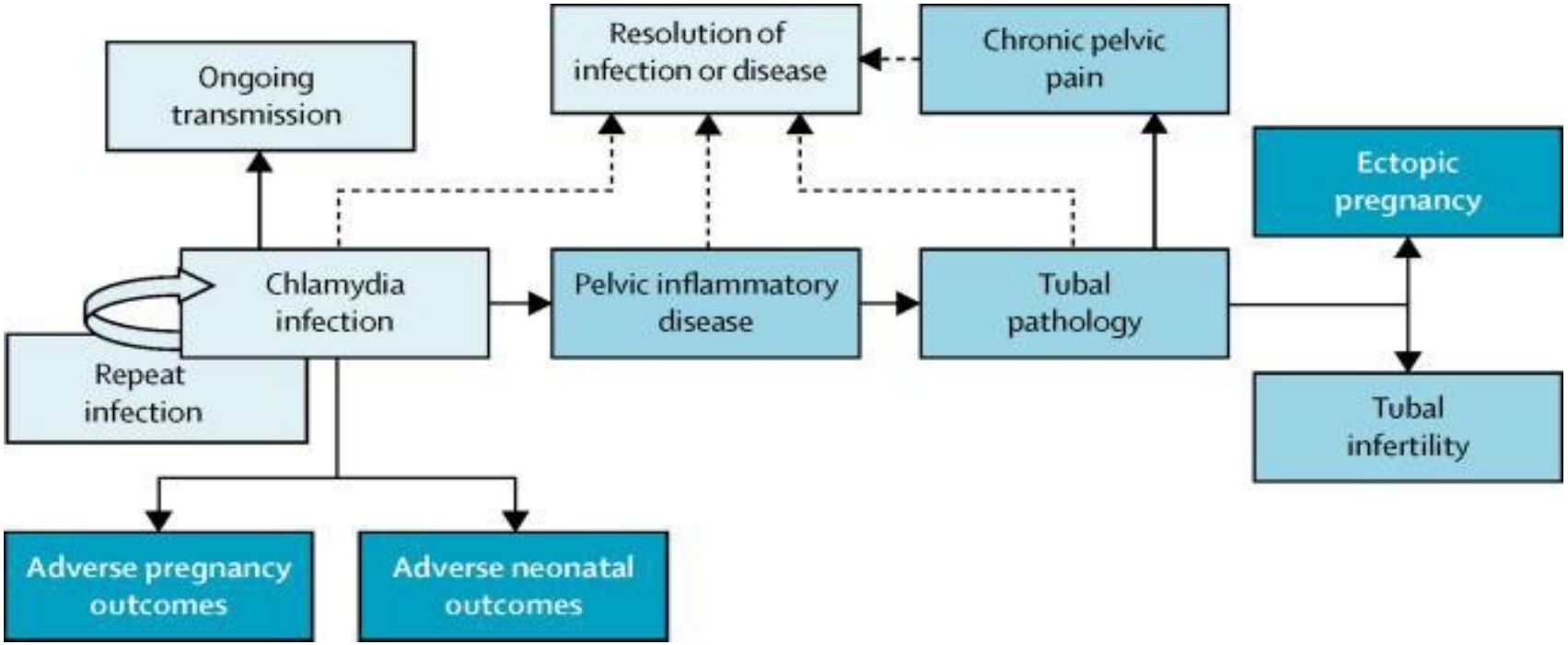
- Perinatally acquired: ↑ likelihood to use condoms (60% use condoms inconsistently); 30% have >1 concurrent partner
- Non-perinatally acquired: continued sexual activity, inconsistent condom use
- Pregnancy desires unchanged

Figure 5. Chlamydia – Rates of Reported Cases by Age Group and Sex, United States, 2017

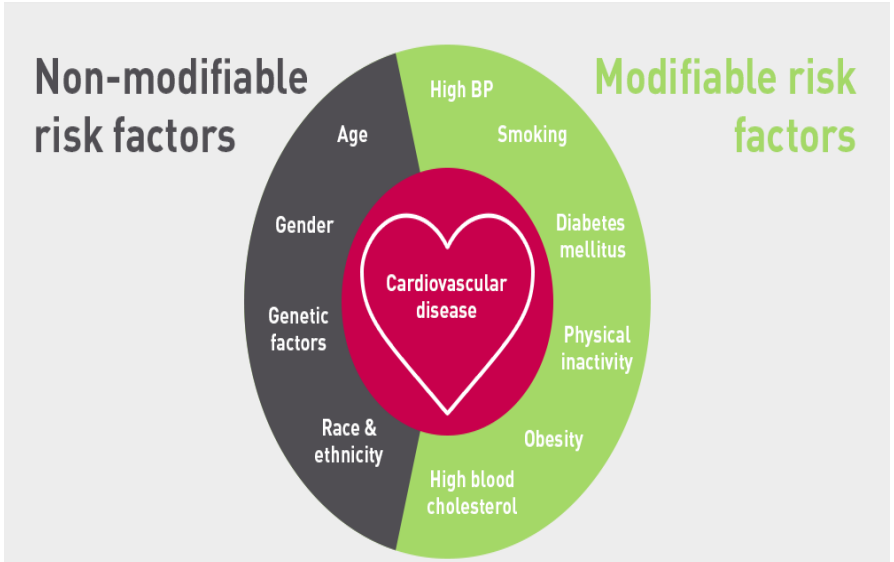


Judd et al PLoS One 2018; Ankunda Pan Afr Med 2016; Koenig JAIDS 2010; CDC

Comorbidities and Sequelae Resulting from STIs



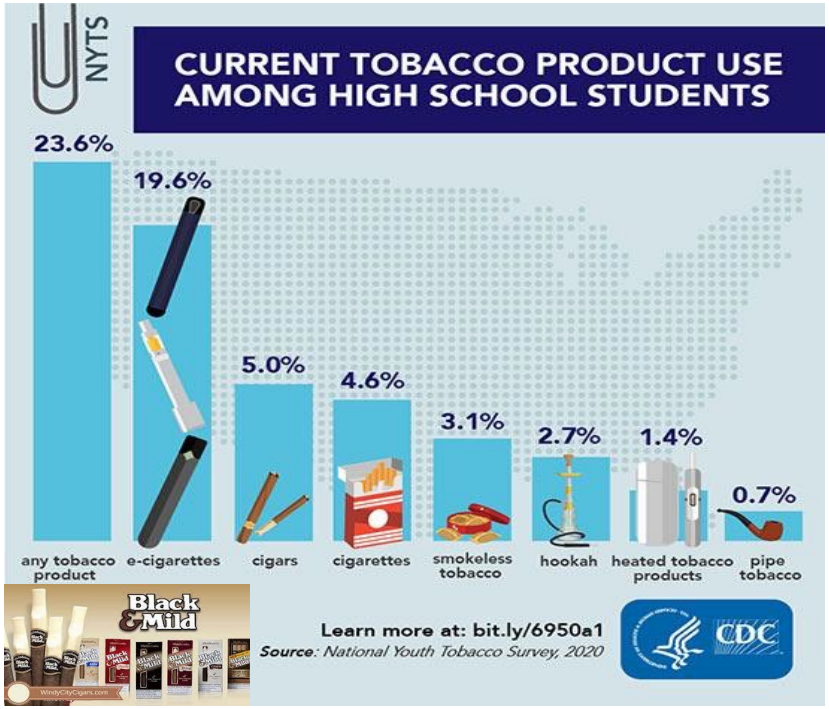
Unemo et al. Lancet ID 2017. 17(8): E235-79



Non-modifiable	Modifiable	Lifestyle	Social
• Age • Gender • Family history of CVD • Ethnicity • Genetic evidence • Previous history of CVD	• Blood pressure • Total cholesterol • HDL cholesterol • Smoking • Blood sugar/diabetes • BMI • Markers of chronic inflammation	• Smoking • Diet • Exercise • Stress	• Income • Social deprivation • Environment

Tobacco use among adolescents

- YHIV: up to 40% report tobacco use
- 20% report daily/almost daily tobacco use

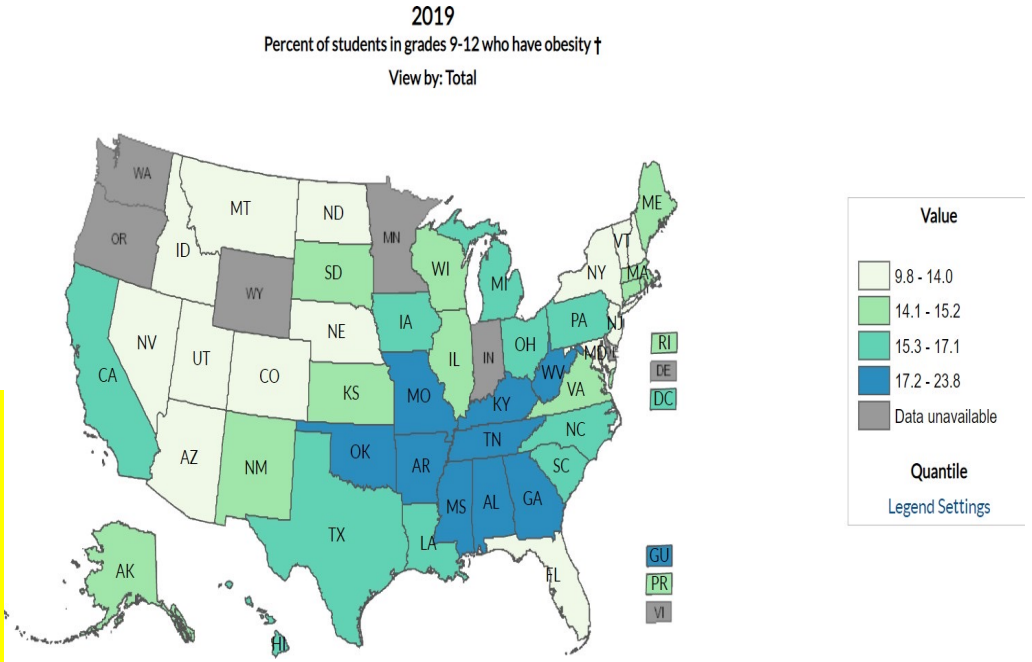


Gamarel AIDS Behav 2018; Nasim et al. Nicotine & Tobacco Research 2016; https://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/index.htm

Obesity

- 21% of 12-19 year olds are obese
  - Hispanic (26%)
  - non-Hispanic Black (24%)
  - non-Hispanic White (16%)

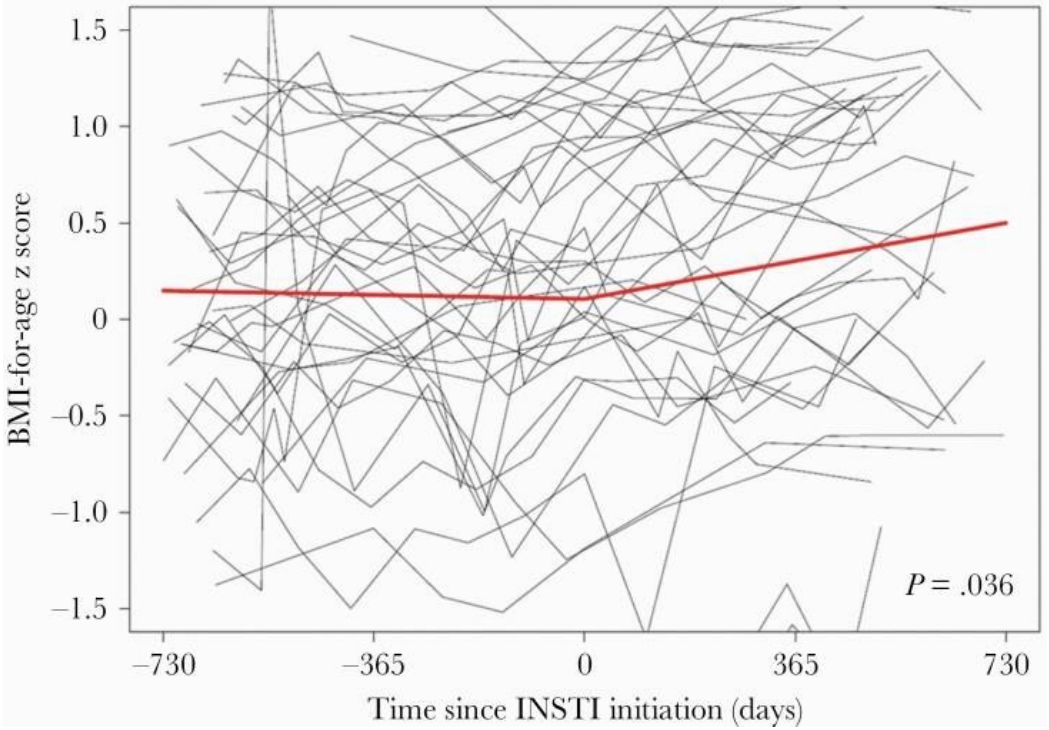
- Obesity among U.S. youth with HIV
  - Overweight/obese (49%)
  - YHIV 10% higher trunk to fat ratio than HEU



Obesity: ≥95th percentile BMI

Jacobson A J Clin Nutrition 2011; Kruzich J Academy of Nutrition and Dietetics 2004; CDC, Youth Risk Behavior Survey 2019

Weight again among adolescents with HIV on INSTIs



Li et al. JPIDS 2020; Koay et al OFID 2021

	2nd Decade 10-19 years	3rd Decade 20-29 years	4th Decade 30-39 years	5th Decade 40-49 years	≥6th Decade ≥50 years
					
	Future Clinical and Research Focus				
Treatment	Developing ideal treatment dosing regimens and formulations	Minimizing polypharmacy, optimizing ART, minimizing drug interactions			
	Long acting antiretroviral therapy, non-ART treatment strategies, HIV cure				
Comorbidities	Longitudinal studies on HIV comorbidities and early biomarkers of organ/systemic dysfunction, prevention strategies				
	Impact of customized mental health screening and interventions				
	Minimizing cognitive dysfunction				

What can you do?

- Take a good history
- Assess risk factors
  - Tobacco
  - Substances
  - Sex
  - Activities
  - Helmets, firearms
- Detailed family history
- Physical examination

Leading Cause of Death in the United States for Select Age Groups (2019)
Data Courtesy of CDC

Rank	10-14	15-24	25-34	35-44	45-54	55-64	All Ages
1	Unintentional Injury 778	Unintentional Injury 11,755	Unintentional Injury 24,516	Unintentional Injury 24,070	Malignant Neoplasms 35,587	Malignant Neoplasms 111,765	Heart Disease 659,041
2	**Suicide 534**	**Suicide 5,954**	**Suicide 8,059**	Malignant Neoplasms 10,695	Heart Disease 31,138	Heart Disease 80,837	Malignant Neoplasms 599,601
3	Malignant Neoplasms 404	Homicide 4,774	Homicide 5,341	Heart Disease 10,499	Unintentional Injury 23,359	Unintentional Injury 24,892	Unintentional Injury 173,040
4	Homicide 191	Malignant Neoplasms 1,388	Malignant Neoplasms 3,577	**Suicide 7,525**	Liver Disease 8,098	CLRD 18,743	CLRD 156,979
5	Congenital Anomalies 189	Heart Disease 872	Heart Disease 3,495	Homicide 3,446	**Suicide 8,012**	Diabetes Mellitus 15,508	Cerebro-vascular 150,005
6	Heart Disease 87	Congenital Anomalies 390	Liver Disease 1,112	Liver Disease 3,417	Diabetes Mellitus 6,348	Liver Disease 14,385	Alzheimer's Disease 121,499
7	CLRD 81	Diabetes Mellitus 248	Diabetes Mellitus 887	Diabetes Mellitus 2,228	Cerebro-vascular 5,153	Cerebro-vascular 12,931	Diabetes Mellitus 87,647
8	Influenza & Pneumonia 71	Influenza & Pneumonia 175	Cerebro-vascular 585	Cerebro-vascular 1,741	CLRD 3,592	**Suicide 8,238**	Nephritis 51,565
9	Cerebro-vascular 48	CLRD 168	Complicated Pregnancy 532	Influenza & Pneumonia 951	Nephritis 2,269	Nephritis 5,857	Influenza & Pneumonia 49,783
10	Benign Neoplasms 35	Cerebro-vascular 158	HIV 486	Septicemia 812	Septicemia 2,176	Septicemia 5,672	**Suicide 47,511**

CLRD: Chronic Lower Respiratory Disease

Note: Suicide is not among the ten leading causes of death among children in the 0-9 year age group nor in adults in the age group 65 years and older.

What can you do?

- **Education** (patient and staff)
- **Counseling**
  - Nutrition
  - Exercise
  - Tob/nicotine (cigarettes, vape, cigarillos, e-cigs)
  - Substance, ETOH use
  - Sex
  - Etc
- **Screening:** BP, lipids (fasting/non- fasting), glucose, weight

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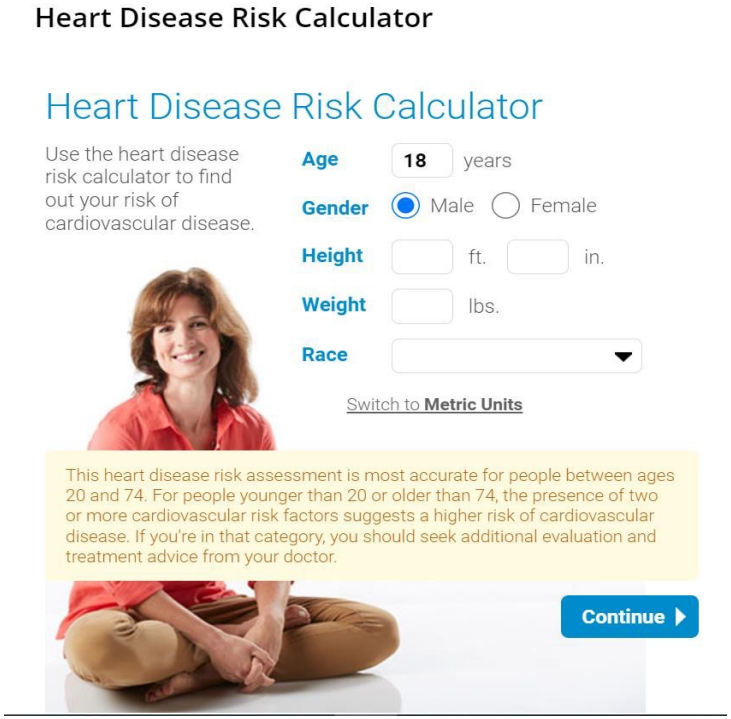
Risk calculators for adolescents?

- ASCVD Heart Risk Calculator (age 40-79)
- If you know your lipids information and you are <60, the Framingham Heart Study General Cardiovascular Disease 30-Year Lipid-Based Risk Score Calculator is used. FOR AGES 30-79
- If you don't know your lipids information and you are <60, the Framingham Heart Study General Cardiovascular Disease 30-Year BMI-Based Risk Score Calculator is used. FOR AGES 30-79
- If you know your lipids information and you are ≥60 or older, the ACC/AHA Pooled Cohort Equations CV Risk Calculator is used.
- If you don't know your lipids information and you ≥ 60 or older, the Framingham Heart Study Cardiovascular Disease 10-Year BMI-Based Risk Score Calculator is used.



http://www.cvriskcalculator.com/; https://www.mayoclinichealthsystem.org/locations/menomonie/services-and-treatments/cardiology/heart-disease-risk-calculator

What can you do?

- **Actions:**
  - Smoking cessation
  - Lifestyle modification
  - Treatment
    - HTN (<130/80 goal) or <90th percentile
    - Hyperlipidemia: ?? (benefit for older youth with clear abnormal)
  - Weight loss
  - hyperlipidemia
  - Substance use treatment
  - STI counseling, screening, and treatment; family planning
  - Immunizations

Immunizations for Adolescents and Young Adults

Human Papilloma (HPV)

Hepatitis A

Hepatitis B

Tdap

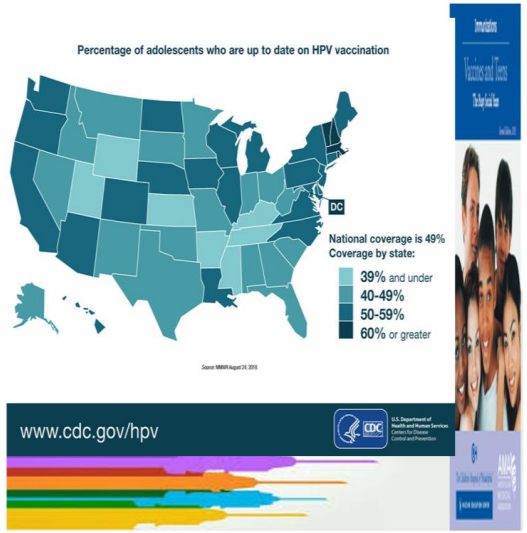
MCV

Flu

COVID

PCV & PS23

Others as indicated



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Conclusion

- Adolescents with HIV (perinatally or non-perinatally acquired) are surviving into adulthood
- Providers must be aware of potential comorbidities that may arise in adolescence
- Critically important to screen for and address comorbidities with prevention and early treatment.

Question-and-Answer Session

2021 Ryan White HIV/AIDS Program CLINICAL CONFERENCE