THE AMERICAN ACADEMY OF HIV MEDICINE www.aahivm.org DECEMBER 2019
Patient Care, Practice Management & Professional Development Information for HIV Care Providers

HIV Specialist

The Future of HIV Prevention and Treatment for Youth

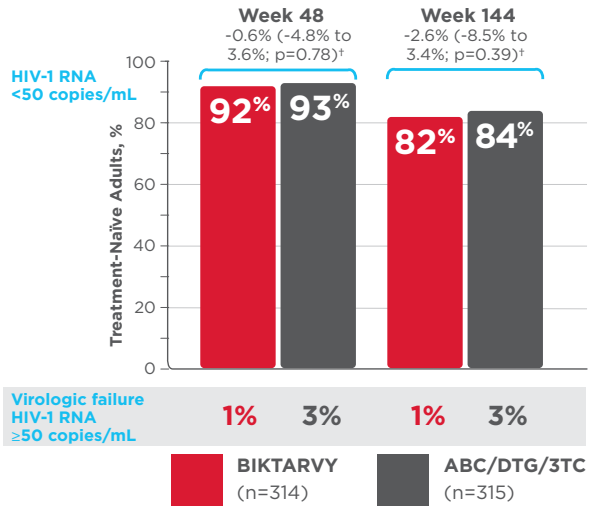
DURABLE POWER AT WEEK 144

BIKTARVY® (bictegravir 50 mg, emtricitabine 200 mg, and tenofovir alafenamide 25 mg) combines the FTC/TAF* backbone with bictegravir, a novel and unboosted INSTI—for a powerful STR[1,2]

Long-term efficacy in treatment-naïve adults at Week 144[2-7]

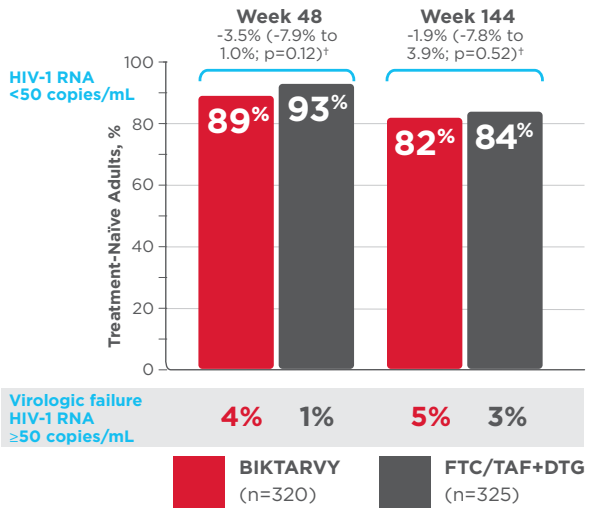
Results noninferior to comparators

Study 1489: Virologic Response



†95% confidence interval.

Study 1490: Virologic Response



†95% confidence interval.

Pivotal treatment-naïve study designs[2-7]:

The efficacy and safety of BIKTARVY for treatment-naïve adults were evaluated in Studies 1489 and 1490. In **Study 1489**, a phase 3, randomized, double-blind, active-controlled study, treatment-naïve adults with an eGFR ≥50 mL/min were randomized in a 1:1 ratio to receive either BIKTARVY (n=314) or ABC/DTG/3TC (n=315) once daily. In **Study 1490**, a phase 3, randomized, double-blind, active-controlled study, treatment-naïve adults with an eGFR ≥30 mL/min were randomized in a 1:1 ratio to receive either BIKTARVY (n=320) or FTC/TAF+DTG (n=325) once daily. **The primary endpoint for both trials was the proportion of adults with HIV-1 RNA <50 copies/mL at Week 48. Secondary endpoints included efficacy, safety, and tolerability through Week 96 and Week 144.**

Most common adverse reactions (incidence ≥5%; all grades) in clinical studies through Week 144 were diarrhea (6%), nausea (6%), and headache (5%).[5]

INDICATION

BIKTARVY is indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥25 kg who have no antiretroviral (ARV) treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known resistance to any component of BIKTARVY.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- **Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of BIKTARVY. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue BIKTARVY. If appropriate, anti-hepatitis B therapy may be warranted.**

#1 PRESCRIBED REGIMEN FOR HIV-1 TREATMENT
Source: Ipsos Healthcare US HIV Therapy Monitor & Scope Study May-July 2019.

Learn more about the BIKTARVY 144 week data at BIKTARVY144.com

No treatment-emergent resistance associated with BIKTARVY through Week 144[2-7]

0 CASES OF RESISTANCE WITH BIKTARVY

In two large phase 3 clinical trials in treatment-naïve adults

- Among 634 treatment-naïve adults in Studies 1489 and 1490, 8 treatment-failure subjects were tested and no amino acid substitutions emerged that were associated with BIKTARVY resistance

IMPORTANT SAFETY INFORMATION (cont'd)

Contraindications

- **Coadministration:** Do not use BIKTARVY with dofetilide or rifampin.

Warnings and precautions

- **Drug interactions:** See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during BIKTARVY therapy and monitor for adverse reactions.
- **Immune reconstitution syndrome,** including the occurrence of autoimmune disorders with variable time to onset, has been reported.
- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. In clinical trials of BIKTARVY, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate BIKTARVY in patients with estimated creatinine clearance (CrCl) <30 mL/min. Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue BIKTARVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.
  Renal monitoring: Prior to or when initiating BIKTARVY and during therapy, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, assess serum phosphorus.
- **Lactic acidosis and severe hepatomegaly with steatosis:** Fatal cases have been reported with the use of nucleoside analogs, including FTC and TDF. Discontinue BIKTARVY if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

Please see Brief Summary of full Prescribing Information for BIKTARVY, including BOXED WARNING, on the following pages.

BIKTARVY®
bictegravir 50mg/emtricitabine 200mg/
tenofovir alafenamide 25mg tablets

*emtricitabine 200 mg/tenofovir alafenamide 25 mg.

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse reactions

- **Most common adverse reactions** (incidence ≥5%; all grades) in clinical studies through week 144 were diarrhea (6%), nausea (6%), and headache (5%).

Drug interactions

- **Prescribing information:** Consult the full prescribing information for BIKTARVY for more information on Contraindications, Warnings, and potentially significant drug interactions, including clinical comments.
- **Enzymes/transporters:** Drugs that induce P-gp or induce both CYP3A and UGT1A1 can substantially decrease the concentration of components of BIKTARVY. Drugs that inhibit P-gp, BCRP, or inhibit both CYP3A and UGT1A1 may significantly increase the concentrations of components of BIKTARVY. BIKTARVY can increase the concentration of drugs that are substrates of OCT2 or MATE1.
- **Drugs affecting renal function:** Coadministration of BIKTARVY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC and tenofovir and the risk of adverse reactions.

Dosage and administration

- **Dosage:** Patients weighing ≥25 kg: 1 tablet taken once daily with or without food.
- **Renal impairment:** Not recommended in patients with CrCl <30 mL/min.
- **Hepatic impairment:** Not recommended in patients with severe hepatic impairment.
- **Prior to or when initiating:** Test patients for HBV infection.
- **Prior to or when initiating, and during treatment:** As clinically appropriate, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, assess serum phosphorus.

Pregnancy and lactation

- **Pregnancy:** There is insufficient human data on the use of BIKTARVY during pregnancy. Dolutegravir, another integrase inhibitor, has been associated with neural tube defects. Discuss the benefit-risk of using BIKTARVY during pregnancy and conception. An Antiretroviral Pregnancy Registry (APR) has been established. Available data from the APR for FTC shows no difference in the rates of birth defects compared with a US reference population.
- **Lactation:** Women infected with HIV-1 should be instructed not to breastfeed, due to the potential for HIV-1 transmission.

Please see Brief Summary of full Prescribing Information for BIKTARVY, including BOXED WARNING, on the following pages.

3TC, lamivudine; ABC, abacavir; DHHS, Department of Health and Human Services; DTG, dolutegravir; eGFR, estimated glomerular filtration rate; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; STR, single-tablet regimen; TAF, tenofovir alafenamide.

References: 1. Tsiang M, Jones GS, Goldsmith J, et al. Antiviral activity of bictegravir (GS-9883), a novel potent HIV-1 integrase strand transfer inhibitor [...]. *Antimicrob Agents Chemother.* 2016;60(12):7086-7097. **2.** BIKTARVY [package insert]. Foster City, CA: Gilead Sciences, Inc.; 2019. **3.** Stellbrink HJ, Arribas JR, Stephens JL, et al. Co-formulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *Lancet HIV.* 2019;6(6):e364-e372. **4.** Wohl DA, Yazdanpanah Y, Baumgarten A, et al. Bictegravir combined with emtricitabine and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection: week 96 results from a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *Lancet HIV.* 2019;6(6):e355-e363. **5.** Data on file. Gilead Sciences, Inc. **6.** Gallant J, Lazzarin A, Mills A, et al. Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial. *Lancet.* 2017;390(10107):2063-2072. **7.** Sax PE, Pozniak A, Montes ML, et al. Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380-1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *Lancet.* 2017;390(10107):2073-2082. **8.** US Department of Health and Human Services. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. http://aidsinfo.nih.gov/contentfiles/adultandadolescentgl.pdf. Updated July 10, 2019. Accessed July 10, 2019.

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BIKTARVY®
bictegravir 50mg/emtricitabine 200mg/
tenofovir alafenamide 25mg tablets

BIKTARVY® (bictegravir 50 mg, emtricitabine 200 mg, and tenofovir alafenamide 25 mg) tablets, for oral use

Brief Summary of full Prescribing Information. See full Prescribing Information. Rx only.

WARNING: POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of BIKTARVY. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue BIKTARVY. If appropriate, anti-hepatitis B therapy may be warranted [*see Warnings and Precautions*].

INDICATIONS AND USAGE

BIKTARVY is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and pediatric patients weighing ≥25 kg who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of BIKTARVY.

DOSAGE AND ADMINISTRATION

Also see ***Warnings and Precautions*** and ***Use in Specific Populations***.

Testing Prior to or When Initiating: Test patients for HBV infection.

Testing Prior to or When Initiating, and During Treatment: As clinically appropriate, assess serum creatinine, estimated creatinine clearance (CrCl), urine glucose, and urine protein in all patients. In patients with chronic kidney disease, assess serum phosphorus.

Dosage: One tablet taken once daily with or without food in patients weighing ≥25 kg.

Renal Impairment: BIKTARVY is not recommended in patients with CrCl <30 mL/min.

Hepatic Impairment: BIKTARVY is not recommended in patients with severe hepatic impairment.

CONTRAINDICATIONS

Also see ***Drug Interactions***.

BIKTARVY is contraindicated to be co-administered with:

- dofetilide due to the potential for increased dofetilide plasma concentrations and associated serious and/or life-threatening events
- rifampin due to decreased BIC plasma concentrations, which may result in the loss of therapeutic effect and development of resistance to BIKTARVY

WARNINGS AND PRECAUTIONS

Also see ***BOXED WARNING***, ***Contraindications***, ***Adverse Reactions***, and ***Drug Interactions***.

Severe Acute Exacerbation of Hepatitis B in Patients Coinfected with HIV-1 and HBV: Patients with HIV-1 should be tested for the presence of chronic hepatitis B virus (HBV) before or when initiating ARV therapy. Severe acute exacerbations of hepatitis B (e.g., liver decompensation and liver failure) have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing FTC and/or TDF, and may occur with discontinuation of BIKTARVY. Patients coinfected with HIV-1 and HBV who discontinue BIKTARVY should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, anti-hepatitis B therapy may be warranted, especially in patients with advanced liver disease or cirrhosis since post-treatment exacerbation of hepatitis may lead to hepatic decompensation and liver failure.

Risk of Adverse Reactions (ARs) or Loss of Virologic Response Due to Drug Interactions: Coadministration of BIKTARVY with certain other drugs may result in known or potentially significant drug interactions; this may lead to loss of efficacy and development of resistance to BIKTARVY or clinically significant ARs from greater exposures of concomitant drugs. Consider the potential for drug interactions and review concomitant medications prior to and during therapy. Monitor for ARs associated with concomitant drugs.

Immune Reconstitution Syndrome (IRS): IRS has been reported in patients treated with combination ARV therapy. During the initial phase of treatment, patients whose immune systems respond may develop an inflammatory response to indolent or residual opportunistic infections, which may necessitate further evaluation and treatment. Autoimmune disorders have been reported to occur in the setting of immune reconstitution; the time to onset is variable, and can occur many months after initiation of treatment.

New Onset or Worsening Renal Impairment: Renal impairment, including acute renal failure and Fanconi syndrome, has been reported with the use of tenofovir prodrugs in animal studies and human trials. In clinical trials of BIKTARVY in subjects with no ARV treatment history with eGFRs >30 mL/min, and in virologically suppressed subjects switched to BIKTARVY with eGFRs >50 mL/min, renal serious adverse events were encountered in <1% of subjects treated with BIKTARVY through Week 48. BIKTARVY is not recommended in patients with CrCl <30 mL/min. Patients taking tenofovir prodrugs who have renal impairment and/or are taking nephrotoxic agents including NSAIDs are at increased risk of developing renal-related ARs. Discontinue BIKTARVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. ***Renal Monitoring:*** Prior to or when initiating BIKTARVY, and during treatment with BIKTARVY, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, assess serum phosphorus.

Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including FTC and TDF. Treatment with BIKTARVY should be suspended in any individual who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

ADVERSE REACTIONS

Also see ***BOXED WARNING*** and ***Warnings and Precautions***.

In Adults with No ARV Treatment History:

The safety assessment of BIKTARVY is based on Week 48 data from two randomized, double-blind, active-controlled trials: 1489 (n=314) and 1490 (n=320), in HIV-1 infected, ARV treatment-naïve adults. Through Week 48, 1% of subjects discontinued BIKTARVY due to adverse events, regardless of severity.

Adverse Reactions: ARs (all Grades) reported in ≥2% of subjects receiving BIKTARVY through Week 48 in Trials 1489 and 1490, respectively were: diarrhea (6%, 3%), nausea (5%, 3%), headache (5%, 4%), fatigue (3%, 2%), abnormal dreams (3%, <1%), dizziness (2%, 2%), and insomnia (2%, 2%). Additional ARs (all Grades) occurring in <2% of subjects administered BIKTARVY in Trials 1489 and 1490 included vomiting, flatulence, dyspepsia, abdominal pain, rash, and depression. Suicidal ideation, suicide attempt, and depression suicidal occurred in <1% of subjects administered BIKTARVY; all events were serious and primarily occurred in subjects with a preexisting history of depression, prior suicide attempt, or psychiatric illness.

Laboratory Abnormalities: Laboratory abnormalities (Grades 3–4) occurring in ≥2% of subjects receiving BIKTARVY through Week 48 in Trials 1489 or 1490, respectively were: amylase >2.0 x ULN (2%, 2%), ALT >5.0 x ULN (1%, 2%), AST >5.0 x ULN (2%, 1%), Creatine Kinase ≥10.0 x ULN (4%, 4%), Neutrophils <750 mm^3 (2%, 2%), and fasted LDL-cholesterol >190 mg/dL (2%, 3%).

Changes in Serum Creatinine: Increases in serum creatinine occurred by Week 4 of treatment and remained stable through Week 48. In Trials 1489 and 1490, median serum creatinine increased by 0.10 mg/dL from baseline to Week 48 in the BIKTARVY group and was similar to the comparator groups.

Changes in Bilirubin: In Trials 1489 and 1490, total bilirubin increases were observed in 12% of subjects administered BIKTARVY through Week 48.

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In Virologically Suppressed Adults: The safety of BIKTARVY in HIV-1 infected, virologically suppressed adults is based on Week 48 data from 282 subjects in a randomized, double-blind, active-controlled trial in which virologically suppressed subjects were switched from either DTG + ABC/3TC or ABC/DTG/3TC to BIKTARVY; and Week 48 data from 290 subjects in an open-label, active-controlled trial in which virologically suppressed subjects were switched from a regimen containing atazanavir (given with cobicistat or ritonavir) or darunavir (given with cobicistat or ritonavir) plus either FTC/TDF or ABC/3TC, to BIKTARVY.

Adverse Reactions: Overall, the safety profile in virologically suppressed adult subjects was similar to that in subjects with no antiretroviral treatment history.

In Virologically Suppressed Pediatric Subjects: The safety of BIKTARVY was evaluated in HIV-1 infected, virologically suppressed subjects between the ages of 12 to <18 years and weighing ≥35 kg (N=50) through Week 48, and in virologically-suppressed subjects between the ages of 6 to <12 years and weighing ≥25 kg (N=50) through Week 24 in an open label clinical trial.

Adverse Reactions: No new ARs or laboratory abnormalities were identified compared to those observed in adults. ARs were reported in 10% of pediatric subjects. The AR reported by more than one subject was abdominal pain (n=2). One subject (1%) had Grade 2 ARs of insomnia and anxiety that led to discontinuation of BIKTARVY. The other ARs that occurred in single subjects were similar to those seen in adults.

DRUG INTERACTIONS

Also see ***Indications and Usage***, ***Contraindications***, and ***Warnings and Precautions***.

Other Antiretroviral Medications: BIKTARVY is a complete regimen for the treatment of HIV-1 infection, BIKTARVY coadministration with other ARV medications for treatment of HIV-1 infection is not recommended. Complete information regarding potential drug interactions with other ARV medications is not provided.

Potential for BIKTARVY to Affect Other Drugs: BIC inhibits organic cation transporter 2 (OCT2) and multidrug and toxin extrusion transporter 1 (MATE1) *in vitro*. Coadministration of BIKTARVY with drugs that are substrates of OCT2 and MATE1 (e.g., dofetilide) may increase their plasma concentrations.

Potential Effect of Other Drugs to Affect BIKTARVY: BIC is a substrate of CYP3A and UGT1A1. A drug that is a strong inducer of CYP3A and also an inducer of UGT1A1 can substantially decrease the plasma concentrations of BIC which may lead to loss of efficacy and development of resistance. The use of BIKTARVY with a drug that is a strong inhibitor of CYP3A and also an inhibitor of UGT1A1 may significantly increase the plasma concentrations of BIC. TAF is a substrate of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). Co-administration of drugs that inhibit P-gp and BCRP may increase the absorption and plasma concentrations of TAF. Co-administration of drugs that induce P-gp activity are expected to decrease the absorption of TAF, resulting in decreased plasma concentration of TAF, which may lead to loss of efficacy and development of resistance.

Drugs Affecting Renal Function: Because FTC and tenofovir are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion, coadministration of BIKTARVY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC, tenofovir, and other renally eliminated drugs, which may increase the risk of ARs.

Established and Potentially Significant Drug Interactions: The listing of established or potentially clinically significant drug interactions with recommended prevention or management strategies described are based on studies conducted with either BIKTARVY, the components of BIKTARVY (BIC, FTC, and TAF) as individual agents, or are drug interactions that may occur with BIKTARVY. **An alteration in regimen may be recommended.**

- Antiarrhythmics: dofetilide. Coadministration is contraindicated due to potential for serious and/or life-threatening events.
- Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin. Coadministration with alternative anticonvulsants should be considered.
- Antimycobacterials: rifampin. Coadministration is contraindicated due to the effect on BIKTARVY. Rifabutin, rifapentine. Coadministration is not recommended.
- Herbal Products: St. John's wort. Coadministration is not recommended.
- Medications/oral supplements containing polyvalent cations (e.g., Mg, Al, Ca, Fe): Antacids containing Al/Mg: BIKTARVY can be taken at least 2 hours before or 6 hours after taking antacids containing Al/Mg. Routine administration of BIKTARVY together with, or 2 hours after, antacids containing Al/Mg is not recommended. Supplements or antacids containing Ca or Fe: BIKTARVY and supplements or antacids containing Ca or Fe can be taken together with food. Routine administration of BIKTARVY under fasting conditions together with, or 2 hours after, supplements or antacids containing Ca or Fe is not recommended.
- Metformin: Refer to the prescribing information of metformin for assessing the benefit and risk of concomitant use of BIKTARVY and metformin.

Consult the full Prescribing Information prior to and during treatment with BIKTARVY for important drug interactions; this list is not all inclusive.

USE IN SPECIFIC POPULATIONS

Also see *Dosage and Administration*, *Warnings and Precautions*, and *Adverse Reactions*.

Pregnancy: *Pregnancy Exposure Registry:* There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to BIKTARVY during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263. *Risk Summary:* There are insufficient human data on the use of BIKTARVY during pregnancy to inform a drug-associated risk of birth defects and miscarriage. Dolutegravir, another integrase inhibitor, has been associated with neural tube defects. Discuss the benefit-risk of using BIKTARVY with individuals of childbearing potential, particularly if pregnancy is being planned. BIC and TAF use in women during pregnancy has not been evaluated; however, FTC use during pregnancy has been evaluated in a limited number of women as reported to the APR. Available data from the APR show no difference in the overall risk of major birth defects for FTC compared with the background rate for major birth defects of 2.7% in a U.S. reference population of the Metropolitan Atlanta Congenital Defects Program. The rate of miscarriage is not reported in the APR.

Lactation: The Centers for Disease Control and Prevention recommend that HIV-infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Based on published data, FTC has been detected in human milk; it is not known whether BIKTARVY or all of the components of BIKTARVY are present in human breast milk, affects human milk production, or has effects on the breastfed infant. BIC was detected in the plasma of nursing rat pups likely due to the presence of BIC in milk, and tenofovir has been shown to be present in the milk of lactating rats and rhesus monkeys after administration of TDF. It is unknown if TAF is present in animal milk. Because of the potential for HIV transmission in HIV-negative infants, developing viral resistance in HIV-positive infants, and ARs in nursing infants, mothers should be instructed not to breastfeed.

Pediatric Use: Clinical studies of BIKTARVY included 50 subjects aged 12 to <18 years and weighing ≥35 kg, and 50 subjects aged 6 to <12 years and weighing ≥25 kg. Safety and effectiveness of BIKTARVY in pediatric patients weighing <25 kg have not been established.

Geriatric Use: Clinical studies of BIKTARVY did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Renal Impairment: BIKTARVY is not recommended in patients with severe renal impairment (CrCl <30ml/min). No dosage adjustment of BIKTARVY is recommended in patients with CrCl >30ml/min.

Hepatic Impairment: No dosage adjustment of BIKTARVY is recommended in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. BIKTARVY is not recommended for use in patients with severe hepatic impairment (Child-Pugh Class C) as BIKTARVY has not been studied in these patients.

OVERDOSAGE:

If overdose occurs, monitor the patient for evidence of toxicity. Treatment consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient.

210251-GS-002 August 2019

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HIV Specialist

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DECEMBER 2019 | Volume 11, No. 4 | **www.aahivm.org**

FEATURES

DEPARTMENTS

By BRUCE J. PACKETT II
Executive Director, AAHIVM

Navigating the World of Adolescence

AS I WAS READING DRAFTS FOR THE GREAT ARTICLES in this edition of *HIV Specialist,* I found myself thinking back to my own adolescence. How prepared was I, between ages 13 and 18, for making "responsible" and safe decisions with regard to my own cis-heteronormative identity and sexuality (and thus comparably very simple to some of the cases you will read about in this issue)? Despite all the privileges of a relatively affluent suburban public education, a generally "liberal" east coast state (with sex-ed policies to match), mostly progressively oriented parents and so on, I found myself – in retrospect – very much still with an unfledged and dubious psyche, ill-equipped to foresee and manage risks of various kinds effectively, inherently suspicious of educators and systems. As an obvious result, I certainly made misjudgments and induced jeopardy along the way. It seems to me that this disposition in adolescence, specifically with regard to nascent identity formation (sexual, gender and otherwise), must be nearly universal.

When we start to peel away those privileges I was afforded, and even add additional societal and personal challenges, it becomes precisely clear why STIs and HIV continue to be remarkable hazards for people in this age group. In our sexual health-focused issue last quarter, we talked a lot about unstable housing, stigma, structural racism and inequality, substance use and mental illness. Those same perils intersect in magnifying proportions with the adolescent brain.

Our guest editor for this issue, Dr. Michelle Collins-Ogle, is an experienced provider of adolescent care. In one of her articles, she underscores the issue of "denial," specifically as it relates to substance use disorder in adolescents. "Denial," uncertainty, stigmatization and social and familial pressures of all kinds as they relate to one's sexual and gender identities and predilections, are all informing the many risk-inducing aspects of adolescent behaviors, and underscore the need for practitioners to communicate effectively with their adolescent patients (and, when appropriate, their parents) on issues of prevention, sexual health and wellness.

Other articles herein focus on issues of transgender patient care, especially in the adolescent population and those attendant considerations. We also look at best practices as it relates to clinical care, how barriers to care and prevention differ for adolescents based upon where they live, and the challenges parents face when talking to their kids about sex.

The common theme throughout is of the need for an integrated educative response to these challenges, from the family, the clinic, the schools and the community. The CDC uses evidence to tell us that routine HIV testing should begin at 13. It is obviously an important marker to bear in mind, but must also be paired with other prevention and sexual health awareness interventions. There is not one model solution to all the challenges, and different settings and specific identities and people require different responses and different pedagogical and infrastructural models and approaches. Despite the diversity, universally, we have to build *trust* into all these models and approaches.

Adolescents present the strongest structural, individual and psychological challenges, but the solutions therefrom will truly pave the path towards ending the HIV epidemic and reducing STIs. If we can meet the complex and uncertain needs of adolescents in these ways, we can expand those lessons to everyone.

The Academy would like to thank Dr. Ogle for her exceptional guidance and contribution to this issue. As a member of the Academy's Board of Directors and in her daily practice, Dr. Ogle is always committed to her role in educating others on the need to optimize the care of our youth. HIV

APPLICATIONS NOW BEING ACCEPTED

GILEAD SCIENCES RESEARCH SCHOLARS PROGRAM IN HIV

Gilead Sciences Research Scholars Program for Cardiovascular Comorbidities

The Gilead Research Scholars Program supports innovative research from emerging investigators around the world to advance scientific knowledge in areas of unmet medical needs and improve the lives of patients everywhere

Each award will be funded up to USD130,000, to be paid in annual installments of up to USD65,000

Awards are subject to separate terms and conditions

SCIENTIFIC REVIEW COMMITTEE

Applications will be reviewed by a Committee of internationally recognized experts in basic and clinical research in the fields of HIV and Cardiovascular Comorbidities

For complete program information and to apply for an award, please visit the website below

http://researchscholars.gilead.com

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In the NEWS

HIV CARE PROVIDERS IDENTIFY THE TOP BARRIERS TO ENDING THE EPIDEMIC

THE AMERICAN ACADEMY of HIV Medicine highlighted critical barriers to ending the HIV epidemic as identified by HIV care providers in the hardest hit areas of the country. The survey participants – made up of AAHIVM members and HIV credentialed providers – reside in the 50 counties, urban jurisdictions and seven rural states identified as initial geographic targets within the Trump Administration's Ending the Epidemic (EtE) initiative. According to respondents, the most urgent challenges include a critical workforce shortage, homelessness/unstable housing, HIV stigma, and transportation barriers.

In the State of the Union Address on February 5, 2019, President Trump announced his Administration's goal to end the HIV epidemic in the United States within 10 years. The stated goals are to reduce new HIV infections in the US by 75% in five years and 90% by 2030.

"The Administration's ambitious goals seem remarkably achievable if you are simply focused on the clinical tools available, such as treatment therapies and prevention options including PrEP," stated Bruce J. Packett II, executive director of AAHIVM. "But this survey tells us that we are not looking at the whole picture. We have to address the real problems and barriers articulated by the people on the ground and in the fight every day, including issues like stigma and unstable housing. Administration officials in charge of fund allocation need to understand the greatest areas of concern in order to maximize results."

AAHIVM conducted an online survey of their membership and credentialed providers specifically in the EtE geographic jurisdictions in July and August of 2019. There were 325 total respondents, representing 10.2 percent response rate among targeted providers in 43 out of the 50 jurisdictions and in all seven states. One quarter of the respondents have been treating people living with HIV for more than 20 years.

Key findings include:

- Nearly half of providers treating patients with HIV have caseloads of over 200 patients currently, and over half of respondents anticipate the HIV patient caseloads to increase over the next 12 months. The few providers who anticipated a decrease in HIV patient caseloads are nearing retirement or leaving the field of HIV medicine. This strongly suggests a critical workforce shortage of clinical providers to treat people with HIV in these high-incidence jurisdictions.
- Providers cite homelessness/unstable housing, HIV stigma, and transportation barriers as the three biggest barriers to care. They also cite the homeless/unstably housed, people with substance use disorders, and people with mental health disorders as the hardest to bring into care; however, long acting agents coming to the market soon may play a role in the ability to treat these populations.
- Across the care continuum, providers in every jurisdiction consistently said their community needed significant improvement on getting pre-exposure prophylaxis (PrEP) into the hands of people who need it the most and who ask for it. Some of the data, especially in the South, point to providers not believing certain populations are at risk for HIV. More education needs to be offered to all health professionals in these areas around the effectiveness of PrEP and how to identify risk.
- Providers' assessment of the local epidemic varies based on their practice setting. Clinicians in private practice and Ryan White Funded clinics typically view their community as better off in terms of their management of the local epidemic than those in Hospitals and Health Center settings.
- The data indicates that the U.S. is experiencing two HIV epidemics. In urban jurisdictions where there is an historical HIV epidemic, clinicians believe their community is faring better across the HIV care continuum, there are more providers available to treat people with HIV and provide PrEP, and there are fewer barriers to care. In jurisdictions where HIV is emerging and in the rural southern states targeted by the EtE, there is a general shortage of clinical providers, pervasive barriers to providing care and community stigma around HIV and its risk factors.

AAHIVM plans to utilize this data as a needs assessment for AAHIVM's education and training activities for providers in 2020 and beyond.

"This data indicates that the Academy needs to continue to provide education and training to support the clinical HIV workforce, but we need to redouble our efforts to ensure that providers are entering the field," stated Packett. "We also look forward to sharing this data with the members of the Administration in hopes of providing insights that can lead to meaningful steps in ending the epidemic."

SHUTTERSTOCK/ROBERT KNESCHKE

SHUTTERSTOCK/ JULIA LAZEBNAYA

HIV Testing, Treatment, Prevention not Reaching Enough Americans

FAR TOO MANY AMERICANS with HIV are unaware that they have it. Far too few have the virus under control through effective treatment. And far too few Americans are taking the daily pill that prevents HIV. The findings – showing that progress in reducing new HIV infections in the United States has stalled in recent years – come in a new CDC Vital Signs report recently published.

The report shows that increasing HIV testing, treatment, and prevention is critical to stopping HIV transmission in the United States. In addition, health disparities must be addressed to achieve the goals of Ending the HIV Epidemic: A Plan for America, a proposed federal initiative to reduce new HIV infections by 90% by 2030.

"The time is now to end HIV in America. We have the right tools, the right data and the right leadership to get this done," said CDC Director Robert R. Redfield, M.D. "Those living with HIV are our best teachers. They are key to helping us reach people where they are so that we can better diagnose and link patients to care." **Highlights from the report include:**

HIV Testing and Treatment in 2017

- About 154,000 people with HIV (14%) were unaware of their status and therefore could not take advantage of HIV treatment to stay healthy, control the virus, and prevent transmitting HIV to others. Young people ages 13 to 24 were less likely to know their HIV status than those age 25 and older.
- Only two-thirds (63%) of those who knew they had HIV had the virus under control through effective treatment. Young people and African Americans were least likely to have the virus under control.

Pre-Exposure Prophylaxis (PrEP) in 2018:

- About 18% (219,700) of the 1.2 million people who could benefit from PrEP, a daily pill that prevents HIV, had received a prescription for the medication. Coverage was especially low among young people, African Americans, and Latinos who could benefit from PrEP.
- This analysis captured data from 92% of all prescriptions from U.S. retail pharmacies, but did not include prescriptions from closed health care systems, such as managed care organizations and military health plans. Therefore, PrEP coverage was likely higher than these estimates.

New HIV Infections:

- CDC estimates that new HIV infections remained relatively stable, at about 38,000 per year, from 2013 to 2017.

If it is funded, the ETE initiative will substantially increase resources, technology, and expertise where they're needed most.

"The number of people who acquire HIV each year is unacceptably high," said Jonathan Mermin, M.D., M.P.H., director of CDC's National Center for HIV/AIDS, Viral Hepatitis, and STD Prevention. "Ending this epidemic would be one of the greatest public health triumphs in our nation's history."

Ready, Set PrEP Launches

The U.S. Department of Health and Human Services (HHS) launched a national program to distribute medications used as pre-exposure prophylaxis to uninsured Americans. The initiative, Ready, Set PrEP, follows up on Gilead Sciences' announcement earlier this year that it would donate 2.4 million bottles of Truvada each year for 11 years. This donation will extend PrEP to 200,000 uninsured parties.

HHS announced the details to apply for free PrEP and has established a new website, www.GetYourPrEP.com where individuals can apply for the free medication. Applicants can also call toll-free to 855-447-8410 and must test negative for HIV, have valid prescription for Truvada, and not have prescription drug coverage. Healthcare providers who are interested in helping patients enroll may also get information at www.getyourprep.com.

Three retail pharmacies, Walgreens, Rite Aid, and CVS Health have also donated their dispensing services and will have medications available no later than March 30. In addition, the retail chains will offer patient counseling services to promote patient adherence.

Ready, Set, PrEP is part of the administrations, Ending the Epidemic plan which aims to reduce new infections in the United States by 75 percent in five years and 90 percent in 10 years. "Ready Set PrEP is a historic expansion of access to HIV prevention medication and a major step forward in President Trump's plan to end the HIV epidemic in America," HHS Secretary Azar said in a release.

Thanks to Ready, Set, PrEP, thousands of Americans who are at risk for HIV will now be able to protect themselves and their communities.

AAHIVM believes that PrEP is an important prevention strategy for ending the HIV epidemic. We encourage our members to share Academy resources including our enduring webinar from the PrEP Grand Rounds Series with 0.75 CME credit ours with medical providers beyond the Academy's network credentialed providers and dues paying members. Combined we can ensure that Ready, Set, PrEP is utilized widely by people without prescription drug coverage and expand access to PrEP.

SHUTTERSTOCK/TIERNEYMJ

In the NEWS

AAHIVM Signs on to GLAAD Letter Calling for Facebook to Remove Anti-PrEP Ads

ON DEC. 9, GLAAD (prior to 2013, known as a the Gay and Lesbian Alliance Against Defamation), released an Open Letter to Facebook calling on its Chair and CEO, Mark Zuckerberg, to remove all Facebook and Instagram messages that "are convincing individuals to avoid PrEP" by claiming that it is "invariably leading to avoidable HIV infections." These misleading ads, the Open Letter states, are "causing significant harm to public health" by "claiming that the drug has caused harmful side effects" among people who use it.

The Open Letter was spearheaded by GLAAD and co-signed by over 50 organizations including the Academy. Last summer, we noticed these ads being posted by personal injury lawyers in increasing numbers. We responded to this issue by developing an easy-to-read fact sheet explaining that these ads are incorrect and urging Academy members to make copies and distribute to their patients and in other venues where they will reach potential PrEP users. The fact sheet is designed to warn Facebook and Instagram users and their communities that these ads are inaccurate and misleading -- and provide them with correct information about the value of PrEP. More copies of this sheet are available for free on request. With HIVMA, the Academy also co-authored a commentary in POZ magazine on the subject.

The messages in the false Facebook ads about PrEP are also extensively contradicted by other sources, including the US Preventive Services Task Force. The USPSTF, a Congressionally-appointed body, approved the use of Truvada for PrEP earlier this year, designating it both safe and effective. This designation enables the ACA to require that it be paid for by most private insurers and Medicaid expansion programs. Unfortunately, this requirement cannot be enacted until one full "plan year" after the USPSTF ruling (which will be 2020 or 2021 for most people – depending on their coverage).

A third recent development contradicting Facebook's decision to allow the ads is the Administration's move to provide low income Americans with free PrEP. On Dec. 3, Health and Human Services Secretary Alex Azar announced that his department would, "with donated drugs and services provided by major pharmacy chains", deliver free Truvada to 200,000 HIV-negative uninsured Americans who needed it. According to Scientific American, Gilead will donate the medication and the government will "cover costs of the program, which include determining if someone who applies is eligible as well as distribution and processing claims."

Whether the anti-PrEP ads appearing on Facebook will discourage individuals targeted to benefit from this Administration's PrEP offer remains to be seen. According to Pew Research Center, however, "lower income teens are more likely than high-income teens to use Facebook." In 2018, 70% of those living in households with $30,000 or less annually versus 36% of those from households with $75,000 annually or more. It is foreseeable that the Facebook ads, if continued, may cripple this attempt to expand PrEP. Lots of people considering the new DHHS program are also likely Facebook and Instagram readers.

SHUTTERSTOCK/ BARS GRAPHICS

Viral Suppression Greater for Those with Qualified Health Plans Through ADAPs

RESEARCH PUBLISHED by Oxford University Press found that PLWH enrolled in an ADAP-funded QHPs were more likely to achieve viral suppression than people on ADAP without enrollment in a QHP. The study by McManus et al. was based on a multistate comparison that included 7,776 participants in total; most of them living in Virginia (59%) and South Carolina (37%), with a few from Nebraska (4.7%). Extrapolating from the data they collected, McManus calculated that, if all 114,394 direct ADAP clients in the United States in 2017 shifted to ADAP-funded QHPs, an additional 5,719 PLWH would potentially achieve VS. If QHP enrollment directly leads to improvements in VS, then this would translate to an additional 2.4% of ADAP patients achieving VS nationally.

McManus decided to examine differences between the experiences of people in the three states where ADAP-funded QHPs coverage was offered and those with "regular" care through Medicaid expansion. She found that those who received ADAP-funded QHP coverage had a viral suppression rate of 86%, while those who received medication directly from an ADAP had a viral suppression rate of 80%.

Based on interviews of the study participants, McManus hypothesized that the PLWH enrolled in a QHP may have experienced viral suppression as a result of one or more of the following: "1) either perceived or actual improved medication coverage, 2) improved method of obtaining medication for those who preferred receiving medications by mail, and 3) increases access to overall healthcare leading to improved engagement in healthcare, including HIV care."

This study suggests that low-income PLWH may benefit more from ADAP-funded Quality Health Plans than through "regular" care provided through Medicaid expansion. If this can be validated with further research, if could help pave the way toward longer and healthier lives. Combined with the new imitative to provide PrEP to those at highest risk, we will hopefully see a decrease in HIV transmission rates as well.

SHUTTERSTOCK/ANDREY POPOV

New Antiretroviral Therapy Linked to Increased Diabetes Risk in North Americans: **Authors Say Monitoring and More Research Needed**

Research presented at the Annual IDWeek Conference and published in Open Forum Infectious Diseases in October looked at increased risk for diabetes among adults starting common antiretroviral therapy (ART) in the United States and Canada.

The study compared 21,516 individuals starting integrase strand inhibitor (INSTI)-based ART, protease inhibitor-based ART or non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART from January 2007 through December 2016 in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). The authors found that that the newer therapies may have an increased risk of diabetes compared to the older NNRTI regimens.

Researchers followed individuals until diabetes was diagnosed, a diabetes specific medication was prescribed or other measure indicating diabetes was recorded, the participant switched regimens or could no longer be contacted. Overall 669 (3%) developed diabetes and among INSTIs raltegravir was associated with a 5-% increased risk of diabetes.

"While more research is needed, this research shows the importance of monitoring for diabetes, hypertension, weight, and other common medical disorders among people living with HIV, and not just viral load control," says co-author Michael Horberg, MD, an HIV specialist with the Mid-Atlantic Permanente Medical Group and director of the Mid-Atlantic Permanente Research Institute.

The findings are compounded by recent data suggesting some of these medications may also contribute to weight gain. While the study indicates an increased risk of developing diabetes for individuals who began ART with INSTI- or PI- vs. NNRTI-based regimens the authors conclude further research is needed to determine whether the increased risk for diabetes can be attributed to weight gain. Dr. Horberg is leading additional research through the Kaiser Permanente HIV Interregional Initiative to better understand the role of these medications in serious clinical outcomes proximal to weight gain.

Abstract available here:

Open Forum Infectious Diseases, Volume 6, Issue Supplement_2, October 2019, Pages S996–S997, https://doi.org/10.1093/ofid/ofz415.2492

Published: 23 October 2019

The Future of HIV Prevention and Treatment for Youth

#Strive2Optimize

BY HASIYA E. YUSUF, MBBS, MPH AND ALLISON L. AGWU, MD, SCM

MICHAEL, NOW 22-YEARS-OLD, WAS FIRST DIAGNOSED WITH HIV at the young age of 17, having acquired the infection from one of his older male sexual partners. Prior to his diagnosis, not unlike many adolescents, he had never been tested for HIV, nor even thought he was at an increased risk. Michael was skipping school, smoking marijuana and couch-surfing having been kicked out of his house after disclosing to his family that he may "like boys." The unexplained symptoms that seemed to emerge from nowhere prompted him to go to the emergency room (He no longer saw his childhood doctor), where he agreed to be tested for HIV, although he did not expect the results to be positive. He was wrong. The test was positive and his CD4 count was only 149/mm^3, and his HIV viral load was over a million copies/mL. Today, Michael is on a triple-drug regimen of antiretroviral therapy (ART) and sees his doctor every three months, which is challenging as he struggles to achieve a school/work balance. Michael has also developed depression about his diagnosis and misses his medication about two times each week when he either forgets to take them or is trying to avoid the occasional side effects.

Michael's story, unfortunately, has been retold in the thousands of young people who continue to acquire HIV annually in the United States.[1] Worldwide, HIV infection among youth is on the rise with more than half of all new infections affecting persons younger than 24.[2] In 2017 alone, nearly a third of new HIV infections in the U.S were recorded in youth and 50 percent of these went undiagnosed. This is substantial considering that in contrast, 85 percent of adults living with HIV are aware of their diagnosis.[1] Furthermore, the burden of HIV in the U.S disparately impacts along racial/ethnic and sexual minority lines, particularly among same-gender loving African American and Latinx males.[3]

Youth with HIV (YHIV) tend to be challenged in reaching HIV treatment goals i.e. viral suppression (undetectable viral load (<200 copies/mL), immune recovery (normalize CD4 count) and reduced risk of HIV transmission. In fact, barely 25 percent of YHIV attain viral suppression.[1] As a demographic group, youth pose a challenge to HIV treatment and the enrollment, retention and viral suppression of YHIV pales significantly in comparison to older adults. The limited uptake of HIV preventive and diagnostic services and the disparate access to HIV treatment observed in YHIV is attributed to a complex interplay of factors ranging from developmental and cognitive stage, social stigma, financial and geographic inaccessibility and youth-unfriendly environments to youth unawareness.[4–7]

In the last three decades, an array of preventive, diagnostic and therapeutic options have emerged, changing the course of HIV for the better.[8–11] Global life expectancy of persons living with HIV (PLWH) rose by 20 to 43 years,[12] and HIV incidence plummeted from 5.6 million infections in 1999 to less than a million in barely two decades.[2,13] Despite the promising trend, HIV risk in young people remains a principal concern, necessitating a shift in focus from simply optimizing existing strategies

ISTOCK/FG TRADE

to exploring new possibilities. As a result, novel research in pursuit of superior alternatives and modalities are forthcoming.[14–16] Hopefully, breakthroughs with newer modalities for both treatment and prevention, driven by the aspiration for an HIV-free future will change the narrative for youth like Michael.

On the social front, open discussions about youth sexuality and sexual orientation remain an uncomfortable dialogue in the U.S. for parents, teachers, healthcare providers and youth themselves, contributing to stigma and inhibiting access to prevention. Open and non-judgmental conversations about sexual behavior is now more critical than ever, given that a third of high school students in the U.S. are sexually active.[17] When youth are seen, minimal time is often spent on sexual history taking.[18] Providers must be taught to engage in effective sexual health discussions with their young patients. This can be achieved through fostering trainings and reeducation for all healthcare providers who come in contact with youth. These affirming discussions are the first step on the continuum toward HIV prevention.

Growing advancements in technology make social media and gaming apps indispensable tools for HIV messaging, youth sexual health education and empowerment. Digital games are rapidly becoming an important tool for improving health behaviors and supporting the delivery of care and education.

HIV prevention is indisputably crucial to controlling HIV in adolescents and young adults. Millions of infections have been averted through abstinence, condom use, behavioral interventions, treatment as prevention (TasP) and more recently, oral pre-exposure prophylaxis (PrEP).[19–21] In spite of its proven efficacy in HIV prevention, oral PrEP has been met with low uptake and adherence especially among youth aged 13 to 24.[22–24] Having identified this drawback, attention is shifting towards long-acting formulations, first popularized by the introduction of injectable, dermal and intrauterine contraceptives.[25]

Presently, long-acting alternatives are utilized in the mental health arena such as with risperidone and paliperidone injections for schizophrenia.[26] The first long-acting PrEP formulation, cabotegravir, an integrase inhibitor, is currently in clinical trials.[27,28] Additionally, HPTN 083, a phase III clinical trial is comparing oral lamivudine/tenofovir with eight weekly cabotegravir injections for possible use as PrEP.[29] The Thai study, a phase III trial of a bivalent gp120 vaccine successfully demonstrated the feasibility of stimulating HIV antibody responses in 97 percent of study subjects.[15] Motivated by its success, a trial on the safety profile and efficacy of a heterologous Clade C gp140 vaccine in preventing HIV-1 infection is ongoing.[14] 10E8.4/iMab bispecific broadly neutralizing antibodies, which effectively prevent HIV infection in macaques monkeys is being studied for HIV treatment and prevention.[16] Microbicides and topical ARVs are not left out as alternatives to oral therapy for gay and bisexual men who have sex with men (GBMSM) and cis/transgender adolescent girls and women.[30,31] Rectal microbicide gels, besides being highly acceptable, exhibit adherence profiles approximating oral PrEP.[32] On the contrary, minimal success was achieved with earlier formulations of vaginal microbicides in younger women due to limited adherence. However, a newer product, a dapivirine vaginal ring is showing greater efficacy of 30 to 50 percent and offers better prospects for adherence.[30] Leveraging the success of long-acting contraceptives through integration with long- acting antiretrovirals for women might also improve adherence.

Growing advancements in technology make social media and gaming apps indispensable tools for HIV messaging, youth sexual health education and empowerment.[33,34] Utilization of Internet applications and blogs for HIV messaging, though still in its nascent stage is demonstrably successful in youth recruitment for HIV testing and PrEP initiation, and with improvement could be transformational for the future.[36]

New strides in HIV diagnostics have enhanced the speed and accuracy at which HIV tests are conducted. Individuals can now perform tests in their homes using over the counter oral swab testing kits.[11]Yet, HIV testing in young people remains low. Only 22 percent of high school students who have ever had sex have been tested for HIV, while rates of STIs are skyrocketing among youth.[37,38] Targeted youth-friendly spaces in addition to universal HIV testing are required for youth engagement, as access to HIV testing for youth is often unrealizable through emergency departments and HIV clinics alone. Therefore, integrating HIV testing into community health centers, school clinics, youth clubs and other spaces where youth are likely to congregate would facilitate enhanced uptake.[39]

YHIV on antiretroviral treatment are seen either in pediatric clinics or by adult-care providers, though the majority tend to be managed by the latter. However, clinical outcomes of HIV treatment in adolescents and young adults enrolled in adult clinics are generally poorer than their adult counterparts in the same clinics.[40,41] This may be due to gaps created by care transition, lapses in communication, poor collaboration between clinics and unfriendly environments for youth in adult clinics.[42] Fluidity between adult and adolescent-care centers promotes better coordination and smoother transitions of care, while we seek to foster youth-friendly environments in both youth and adult-treatment centers.[43]

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Attendance to routine clinic visits remain challenging for YHIV. Missed appointments negatively impact adherence and viral suppression. In response, the use of technological interventions to heighten treatment adherence and decrease frequency of clinic visits is gaining traction. Patients' access to their electronic health records (EHR) and care teams through patient portals allows for the integration of HIV messaging, medication reminders, notification of appointments, access to health records and laboratory results to improve treatment outcomes.[44–46] Further strengthening these portals with video chatting or two-way text/electronic messaging reinforces doctor-patient communication, fosters closer relationships between healthcare providers and patients and builds trust in the system. Innovations through which patients can collect and send blood samples remotely, receive treatment in the mail or drop locations or even by drones which are already in use in different fields of medicine are exciting and worthy of consideration.[47]

In our experience, ascertainment of patients' real-time virologic status and if necessary, alterations to treatment regimens, assessment of adherence barriers and interventions can rarely be made during the visit. This is due to delays in reporting viral load testing which can take days to weeks depending on the center. Faster or even real-time reporting allow for honest real-time discussion of barriers and implementation of interventions. Treatment decisions can be made and implemented on the day of the visit rather than awaiting patient return to the clinic, which for some patient may not happen resulting in missed opportunities to intervene.[48]

Newer drug formulations consisting of single tablet regimens (STRs), smaller pill sizes and a renewed vigor for developing modalities that provide expanded options are progressively changing the HIV-treatment cascade. Integrase inhibitors such as bictegravir and dolutegravir have better pharmacokinetic and pharmacodynamic profiles, and very good tolerability and thus are recommended as first-line treatments for the majority of patient.[49] However, adherence is impacted by a complex web of social, biological, cultural and economic factors and not merely the characteristics of the drugs.[50,51] This is why targeting long-acting formulations and the possibility of a cure, has never been more important. One research consortium, the Long-acting, Extended-release Antiretroviral resource Program (LEAP), is looking to expand the HIV-treatment armamentarium for key populations, youth inclusive, with alternatives such as injectables (e.g., cabotegravir/rilpivirine, capsid inhibitor (GS-6207)), monthly or bimonthly pills (e.g., islatavir (novel NRTI)), dermal patches and implants.[52–55] Judging by the enthusiasm of YHIV toward the prospect of long-acting ART, its acceptability is projected to be very high and these modalities are being assessed in adolescents.[55] Other modalities with diverse immunological targets are also being explored. For example, ibalizumab, a recently approved prototypical CD4 antibody with potentially fewer side effects is recommended for heavily treatment-experienced patients with multi-drug resistance. Several other monoclonal antibodies are at different phases of clinical development.[56] Other strategies including CRiSPR, latency reversal agents and stem cell transplantation are being studied for the possibility of prolonged remissions or cure.[57,58]

Finally, chronic HIV infection is characterized by inflammation, immune activation and accelerated aging, which is

often aggravated by poor viremic control seen commonly in youth.[59] Aging in HIV can be a result of chronic infection, immunological aging or possibly due to the effect of some ARVs[60] and presents with early signs of chronic diseases such as cardiovascular disease, diabetes, dyslipidemias, osteoarthritis and neurological disorders.[61] Comorbidities widen the complexities of HIV management, likely taking a greater toll on the young.[62] By implication, as YHIV grow older, the incidence of chronic diseases is projected to increase.

The impact of aging in YHIV remains an under-researched subject and it is therefore unclear which YHIV are at highest risk for development of co-morbidities and would therefore benefit from preventive interventions. It is vital for providers of youth HIV care to be on the lookout for comorbidities, institute prompt interventions when appropriate and to recommend lifestyle modifications such as exercise and smoking cessation to avert preventable complications. Ideally, development of youth-specific prognostic markers and indicators would help to identify those at highest risk.

Through a combination of well-timed prevention, prompt diagnosis and early initiation of ARVs, Michael's experience would possibly have been mitigated or averted altogether, using current and emerging approaches to HIV prevention and treatment. Future progress, in addition to the knowledge and tools, will improve clinical outcomes and propel society toward an AIDS-free generation. Hopefully, in the not so distant future, experiences like Michael's will become history, not just for youth in the U.S. but globally.

HIV

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REFERENCES

1. HIV Among Youth | Age | HIV by Group | HIV/AIDS | CDC. https://www.cdc.gov/hiv/group/age/youth/index.html. Published April 10, 2019. Accessed June 12, 2019.
2. UNAIDS. HIV Data. 2017.
3. Bekker L-G, Hosek S. HIV and adolescents: focus on young key populations. *J Int AIDS Soc*. 2015;18(2Suppl 1). doi:10.7448/IAS.18.2.20076
4. Krakower DS, Mayer KH. Pre-Exposure Prophylaxis to Prevent HIV Infection: Current Status, Future Opportunities and Challenges. *Drugs*. 2015;75(3):243-251. doi:10.1007/s40265-015-0355-4
5. Mullins TLK, Lehmann CE. Oral Pre-Exposure Prophylaxis (PrEP) for HIV Prevention in Adolescents and Young Adults. *Curr Pediatr Rep*. 2018;6(2):114-122. doi:10.1007/s40124-018-0163-x
6. Whitfield THF, John SA, Rendina HJ, Grov C, Parsons JT. Why I Quit Pre-Exposure Prophylaxis (PrEP)? A Mixed-Method Study Exploring Reasons for PrEP Discontinuation and Potential Re-initiation Among Gay and Bisexual Men. *AIDS Behav*. 2018;22(11):3566-3575. doi:10.1007/s10461-018-2045-1
7. Holloway IW, Dougherty R, Gildner J, et al. Brief Report: PrEP Uptake, Adherence, and Discontinuation Among California YMSM Using Geosocial Networking Applications. *JAIDS J Acquir Immune Defic Syndr*. 2017;74(1):15-20. doi:10.1097/QAI.0000000000001164
8. Eakle R, Venter F, Rees H. Pre-exposure prophylaxis (PrEP) in an era of stalled HIV prevention: Can it change the game? *Retrovirology*. 2018;15(1):29. doi:10.1186/s12977-018-0408-3
9. Siegfried N, Muller M, Volmink J, et al. Male circumcision for prevention of heterosexual acquisition of HIV in men. *Cochrane Database Syst Rev*. 2003;(3):CD003362. doi:10.1002/14651858.CD003362
10. Diamond F. HIV/AIDS treatment drastically reduces mortality and helps limit transmission. *Manag Care Langhorne Pa*. 2018;27(11):16-17.
11. Katz DA, Golden MR, Hughes JP, Farquhar C, Stekler JD. HIV Self-Testing Increases HIV Testing Frequency in High-Risk Men Who Have Sex with Men: A Randomized Controlled Trial. *J Acquir Immune Defic Syndr 1999*. 2018;78(5):505-512. doi:10.1097/QAI.0000000000001709
12. Teeraananchai S, Kerr SJ, Amin J, Ruxrungtham K, Law MG. Life expectancy of HIV-positive people after starting combination antiretroviral therapy: a meta-analysis. *HIV Med*. 2017;18(4):256-266. doi:10.1111/hiv.12421
13. Joint United Nations Programme on HIV / AIDS UNAIDS. AIDS epidemic update: December 1999. *AIDS Anal Afr*. 2000;10(5):2.
14. A Study to Assess the Efficacy of a Heterologous Prime/Boost Vaccine Regimen of Ad26.Mos4.HIV and Aluminum Phosphate-Adjuvanted Clade C gp140 in Preventing Human Immunodeficiency Virus (HIV) -1 Infection in Women in Sub-Saharan Africa - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03060629. Accessed November 27, 2019.
15. Karasavvas N, Billings E, Rao M, et al. The Thai Phase III HIV Type 1 Vaccine Trial (RV144) Regimen Induces Antibodies That Target Conserved Regions Within the V2 Loop of gp120. *AIDS Res Hum Retroviruses*. 2012;28(11):1444-1457. doi:10.1089/aid.2012.0103
16. 10E8.4/iMab Bispecific Antibody in HIV-uninfected and HIV-infected Adults - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03875209. Accessed November 27, 2019.
17. Kann L, McManus T, Harris WA, et al. Youth Risk Behavior Surveillance —United States, 2017. 2018;67(8):479.
18. Alexander SC, Fortenberry JD, Pollak KI, et al. Sexuality Talk During Adolescent Health Maintenance Visits. *JAMA Pediatr*. 2014;168(2):163-169. doi:10.1001/jamapediatrics.2013.4338
19. Effective HIV Prevention Strategies | HIV Risk and Prevention Estimates | HIV Risk and Prevention | HIV/AIDS | CDC. https://www.cdc.gov/hiv/risk/estimates/preventionstrategies.html. Published July 18, 2019. Accessed November 2, 2019.
20. Condoms | HIV Risk and Prevention | HIV/AIDS | CDC. https://www.cdc.gov/hiv/risk/condoms.html. Published February 27, 2018. Accessed October 24, 2019.
21. Krishnaratne S, Hensen B, Cordes J, Enstone J, Hargreaves JR. Interventions to strengthen the HIV prevention cascade: a systematic review of reviews. *Lancet HIV*. 2016;3(7): e307-e317. doi:10.1016/S2352-3018(16)30038-8
22. Kuhns LM, Hotton AL, Schneider J, Garofalo R, Fujimoto K. Use of Pre-exposure Prophylaxis (PrEP) in Young Men Who Have Sex with Men is Associated with Race, Sexual Risk Behavior and Peer Network Size. *AIDS Behav*. 2017;21(5):1376-1382. doi:10.1007/s10461-017-1739-0
23. Strauss BB, Greene GJ, Phillips G, et al. Exploring Patterns of Awareness and Use of HIV Pre-Exposure Prophylaxis among Young Men Who Have Sex with Men. *AIDS Behav*. 2017;21(5):1288-1298. doi:10.1007/s10461-016-1480-0
24. Koss CA, Hosek SG, Bacchetti P, et al. Comparison of Measures of Adherence to Human Immunodeficiency Virus Preexposure Prophylaxis Among Adolescent and Young Men Who Have Sex with Men in the United States. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2018;66(2):213-219. doi:10.1093/cid/cix755

25. Wu JP, Moniz MH, Ursu AN. Long-acting Reversible Contraception-Highly Efficacious, Safe, and Underutilized. *JAMA*. 2018;320(4):397-398. doi:10.1001/jama.2018.8877

26. Lytle S, McVoy M, Sajatovic M. Long-Acting Injectable Antipsychotics in Children and Adolescents. *J Child Adolesc Psychopharmacol*. 2017;27(1):2-9. doi:10.1089/cap.2016.0055

27. Fernandez C, van Halsema CL. Evaluating cabotegravir/rilpivirine long-acting, injectable in the treatment of HIV infection: emerging data and therapeutic potential. *HIVAIDS Auckl NZ*. 2019; 11:179-192. doi:10.2147/HIV.S184642

28. Singh K, Sarafianos SG, Sönnerborg A. Long-Acting Anti-HIV Drugs Targeting HIV-1 Reverse Transcriptase and Integrase. *Pharmaceuticals*. 2019;12(2). doi:10.3390/ph12020062

29. Gulick RM, Flexner C. Long-Acting HIV Drugs for Treatment and Prevention. *Annu Rev Med*. 2019;70(1):137-150. doi:10.1146/annurev-med-041217-013717

30. Baeten JM, Hendrix CW, Hillier SL. Topical Microbicides in HIV Prevention: State of the Promise. *Annu Rev Med*. October 2019. doi:10.1146/annurev-med-090518-093731

31. Friend DR, Kiser PF. Assessment of topical microbicides to prevent HIV-1 transmission: concepts, testing, lessons learned. *Antiviral Res*. 2013;99(3):391-400. doi:10.1016/j.antiviral.2013.06.021

32. Carballo-Diéguez A, Balán IC, Brown W, et al. High levels of adherence to a rectal microbicide gel and to oral Pre-Exposure Prophylaxis (PrEP) achieved in MTN-017 among men who have sex with men (MSM) and transgender women. *PloS One*. 2017;12(7): e0181607. doi: 10.1371/journal.pone.0181607

33. Hightow-Weidman LB, Muessig KE, Bauermeister JA, LeGrand S, Fiellin LE. The Future of Digital Games for HIV Prevention and Care. *Curr Opin HIV AIDS*. 2017;12(5):501-507. doi:10.1097/COH.0000000000000399

34. LeGrand S, Knudtson K, Benkeser D, et al. Testing the Efficacy of a Social Networking Gamification App to Improve Pre-Exposure Prophylaxis Adherence (P3: Prepared, Protected, emPowered): Protocol for a Randomized Controlled Trial. *JMIR Res Protoc*. 2018;7(12). doi:10.2196/10448

35. Lykens J, Pilloton M, Silva C, Schlamm E, Wilburn K, Pence E. Google for Sexual Relationships: Mixed-Methods Study on Digital Flirting and Online Dating Among Adolescent Youth and Young Adults. *JMIR Public Health Surveill*. 2019;5(2): e10695. doi:10.2196/10695

36. Anand T, Nitpolprasert C, Trachunthong D, et al. A novel Online-to-Offline (O2O) model for pre-exposure prophylaxis and HIV testing scale up. *J Int AIDS Soc*. 2017;20(1). doi:10.7448/IAS.20.1.21326

37. Handel MV, Kann L, Olsen EO, Dietz P. HIV Testing Among US High School Students and Young Adults. *Pediatrics*. 2016;137(2). doi:10.1542/peds.2015-2700

38. Sutton MY, Sternberg M, Zaidi A, St. Louis ME, Markowitz LE. Trends in Pelvic Inflammatory Disease Hospital Discharges and Ambulatory Visits, United States, 1985–2001. *Sex Transm Dis*. 2005;32(12):778. doi: 10.1097/01.olq.0000175375. 60973.cb

39. Agwu AL, Quinn TC. Finding Youths at Risk for HIV Infection. *JAMA Pediatr*. 2017;171(6):517-518. doi:10.1001/jamapediatrics.2017.0329

40. Griffith DC, Agwu AL. Caring for youth living with HIV across the continuum: turning gaps into opportunities. *AIDS Care*. 2017;29(10):1205-1211. doi:10.1080/09540121.2017.1290211

SHUTTERSTOCK/NAYPONG STUDIO

Through a combination of well-timed prevention, prompt diagnosis and early initiation of ARVs, Michael's experience would possibly have been mitigated or averted altogether, using current and emerging approaches to HIV prevention and treatment. Future progress, in addition to the knowledge and tools, will improve clinical outcomes and propel society toward an AIDS-free generation.

41. Agwu AL, Siberry GK, Ellen J, et al. Predictors of Highly Active Antiretroviral Therapy Utilization for Behaviorally HIV-1–Infected Youth: Impact of Adult Versus Pediatric Clinical Care Site. *J Adolesc Health*. 2012;50(5):471-477. doi: 10.1016/j.jadohealth.2011.09.001

42. Garvie PA. Transitioning Youth with HIV to Adult HIV Care: Bridging the Gap with Adult Care Clinics for the Life Span. *J Adolesc Health*. 2017;61(4):407-408. doi: 10.1016/j.jadohealth.2017.07.013

43. Philbin MM, Tanner AE, Chambers BD, et al. Transitioning HIV-infected adolescents to adult care at 14 clinics across the United States: Using adolescent and adult providers' insights to create multi-level solutions to address transition barriers. *AIDS Care*. 2017;29(10):1227-1234. doi:10.1080/09540121.2017.1338655

44. McInnes DK, Shimada SL, Midboe AM, et al. Patient Use of Electronic Prescription Refill and Secure Messaging and Its Association with Undetectable HIV Viral Load: A Retrospective Cohort Study. *J Med Internet Res*. 2017;19(2): e34. doi:10.2196/jmir.6932

45. Hightow-Weidman LB, Muessig KE, Bauermeister J, Zhang C, LeGrand S. Youth, Technology and HIV: Recent Advances and Future Directions. *Curr HIV/AIDS Rep*. 2015;12(4):500-515. Doi:10.1007/S11904-015-0280-X

46. Daskalakis, D. (2017). The Electronic Health Record and Patient Portals in HIV. Medicine: Pushing the boundaries of Current Ethics and Stigma. Cambridge Quarterly of Healthcare Ethics, 26(2), 332-336.

47. Rosser JC, Vignesh V, Terwilliger BA, Parker BC. Surgical and Medical Applications of Drones: A Comprehensive Review. *JSLS*. 2018;22(3). Doi:10.4293/JSLS.2018.00018

48. Aziz R. CROI 2019: Point-Of-Care Viral Load testing improves HIV outcomes, researchers say. Science Speaks: Global ID News. https://sciencespeaksblog.org/2019/03/05/croi-2019-point-of-care-viral-load-testing-improves-hiv-outcomes-researchers-say/. Published March 6, 2019. Accessed November 26, 2019.

49. What to Start: Adult and Adolescent ARV. AIDSinfo.2019 https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/11/what-to-start. Accessed November 27, 2019.

50. Kuhns LM, Hotton AL, Garofalo R, et al. An Index of Multiple Psychosocial, Syndemic Conditions Is Associated with Antiretroviral Medication Adherence Among HIV-Positive Youth. *AIDS Patient Care STDs*. 2016;30(4):185-192. doi:10.1089/apc.2015.0328

51. Katz IT, Ryu AE, Onuegbu AG, et al. Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. *J Int AIDS Soc*. 2013;16(3 Suppl 2):18640. doi:10.7448/IAS.16.3.18640

52. Nachman S, Townsend CL, Abrams EJ, et al. Long-acting or extended-release antiretroviral products for HIV treatment and prevention in infants, children, adolescents, and pregnant and breastfeeding women: knowledge gaps and research priorities. *Lancet HIV*. 2019;6(8): e552-e558. doi:10.1016/S2352-3018(19)30147-X

53. Gilead Presents Proof-of-Concept Data for GS-6207, a First-in-Class Capsid Inhibitor, in People Living With HIV. https://www.gilead.com/news-and-press/press-room/press-releases/2019/7/gilead-presents-proofofconcept-data-for-gs6207-a-firstinclass-capsid-inhibitor-in-people-living-with-hiv. Accessed November 27, 2019.

54. Islatravir Clinical Trials, Side Effects. AIDSinfo. 2019. https://aidsinfo.nih.gov/drugs/609/islatravir/0/patient. Accessed November 27, 2019.

55. More Options for Children and Adolescents (MOCHA): Oral and Long-Acting Injectable Cabotegravir and Rilpivirine in HIV-Infected Children and Adolescents - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03497676. Accessed November 27, 2019.

56. Jaworski JP, Cahn P. Preventive and therapeutic features of broadly neutralizing monoclonal antibodies against HIV-1. *Lancet HIV*. 2018;5(12): e723-e731. doi:10.1016/S2352-3018(18)30174-7

57. Didigu C, Doms R. Gene therapy targeting HIV entry. *Viruses*. 2014;6(3):1395-1409. doi:10.3390/v6031395

58. Treatment Action Group. Research towards a cure. 2019. http://www.treatmentactiongroup.org/sites/default/files/Research_toward_a_cure_November_15_2019_final.pdf. Accessed November 27, 2019.

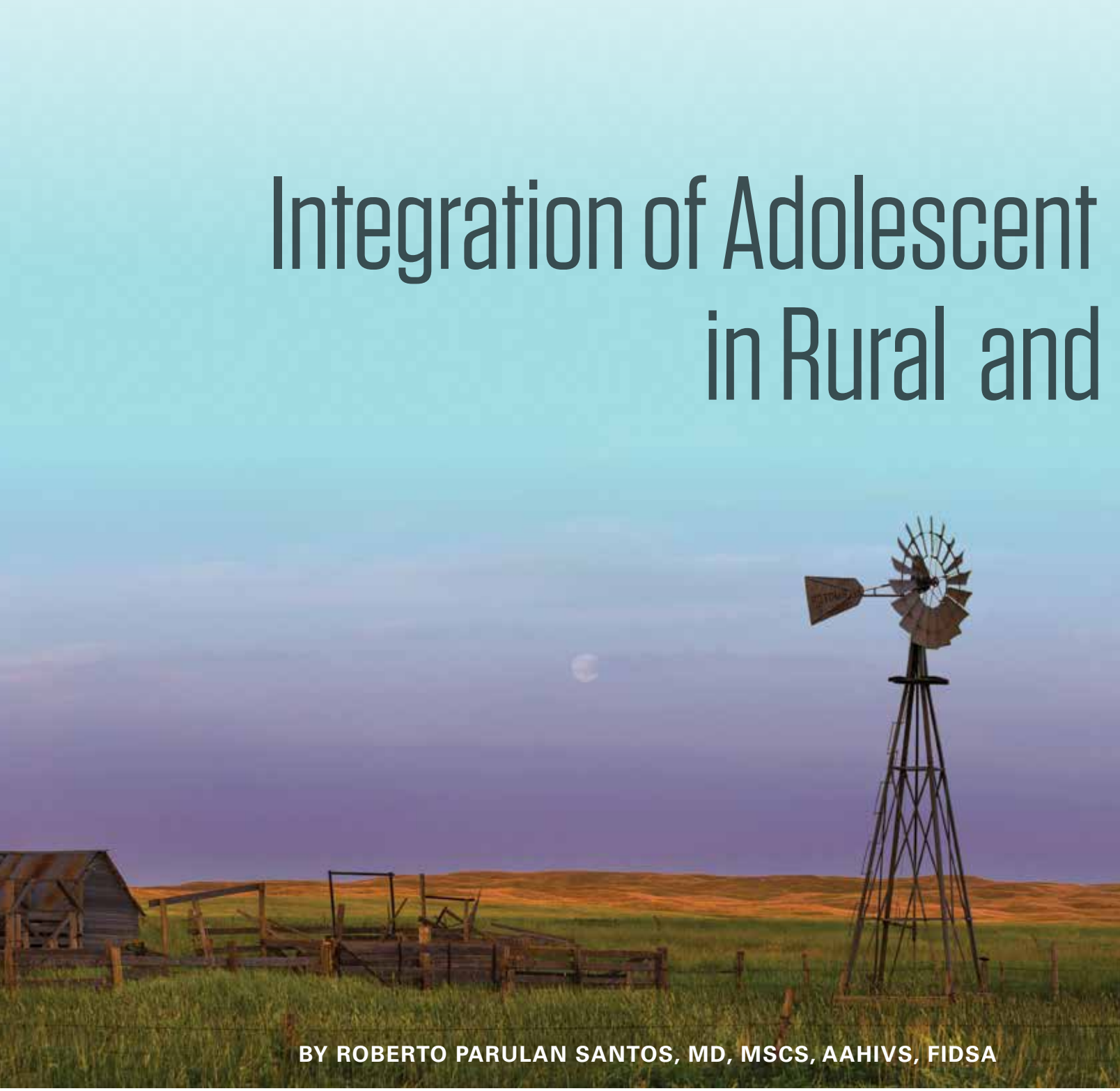
59. Effros RB, Fletcher CV, Gebo K, et al. Aging and infectious diseases: workshop on HIV infection and aging: what is known and future research directions. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2008;47(4):542-553. doi:10.1086/590150

60. Antiretroviral Therapy (ART) in Adolescents and Young Adults with HIV Infection: Overview, Antiretroviral Therapy Considerations, Nucleoside/Nucleotide Reverse Transcriptase Inhibitors. 2019. https://emedicine.medscape.com/article/2041764-overview. Accessed November 2, 2019.

61. Eckard AR, Fowler SL, Haston JC, Dixon TC. Complications of Treatment in Youth with HIV. *Curr HIV/AIDS Rep*. 2016;13(4):226-233. doi:10.1007/s11904-016-0320-1

62. Krentz H, Gill M. Increased costs of HIV care associated with aging in an HIV-infected population. *HIV Med*. 2015;16(1):38-47. doi:10.1111/hiv.12176

Integration of Adolescent in Rural and



BY ROBERTO PARULAN SANTOS, MD, MSCS, AAHIVS, FIDSA

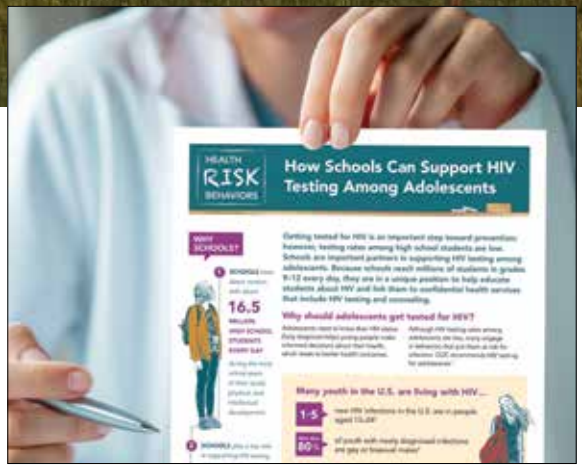
ADOLESCENTS REMAIN ONE OF THE MOST VULNERABLE GROUPS and are most disproportionately affected by HIV infections. In the recent report from Centers for Disease Control and Prevention (CDC) on the 2017 National Youth Risk Behavior Survey, there were several encouraging trends noted which included fewer high school students having sex (48% in 2007 down to 40% in 2017) and fewer students having had four or more sex partners (15% in 2007 down to 10% in 2017).[1] However, there remains some challenges as well including fewer sexually-active students using condoms (62% were using condoms in 2007 down to 54% in 2017).[1] These risky sexual behaviors make adolescents vulnerable to unintended health outcomes like sexually transmitted diseases (STDs).

ISTOCK/KSWINICKI, ERDIKOCAK

Healthcare Services Resource-Limited Communities

In 2017, youth aged 13 to 24 years old comprised more than 20 percent of the approximately 39,000 new HIV diagnoses in the U.S.[2] The rates of adolescents with the diagnosis of HIV infection by state with at least 16 per 100,000 persons are mainly in the southern U.S. from Texas to North Carolina.[3] (Figure 1) Similar patterns are seen in the rates of young adults with HIV infection with at least 164 per 100,000 persons aged 20 to 24 years old living in the southern U.S.[3] (Figure 2)

HIV testing remains at the crux of "Ending the HIV Epidemic (EtHE)".[4] How can at-risk adolescents and young



The GYT campaign is intended to educate the youth on HIV and STDs as well as prevention, connecting adolescents to testing and counseling services and promoting open discussions with healthcare providers, peers and their partners.

Figure 1. Rates of HIV Infections Among Adolescents Ages 13 to 19 Years old (Adapted from CDC)

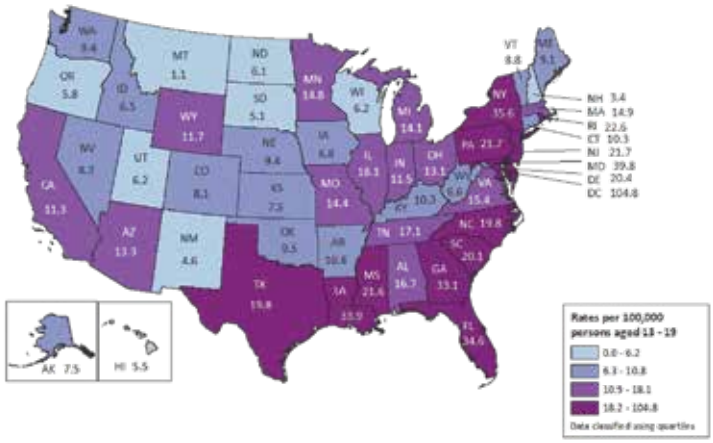


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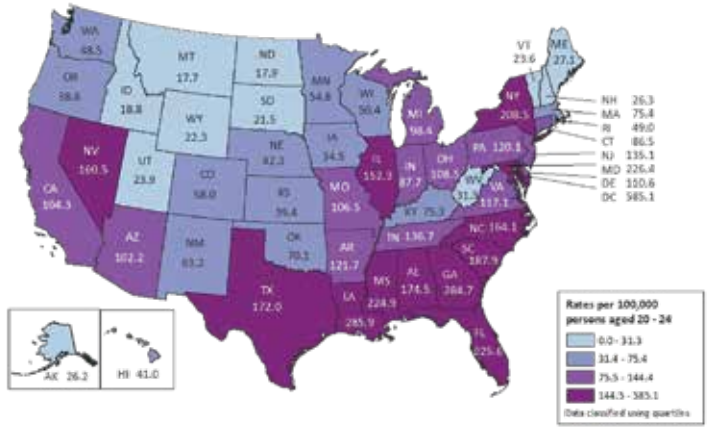
Figure 2. Rates of HIV Infections Among Young Adults Ages 20 to 24 Years old (Adapted from CDC)



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adults prevent HIV infection or be linked to care if they don't know their HIV statuses? In 2006, CDC recommended routine screening for HIV infection in all healthcare settings for all patients aged 13 to 64 years old.[5] A decade later, in 2016, of the estimated 50,900 youth living with HIV, only 56% were aware of their diagnoses. Compared to other age groups, young people were less likely to be aware of their HIV infection.[2] In the U.S., nine percent of high school students had never been tested for HIV which varied from only 8.2 percent to 23.8 percent in those states with available data.[1] HIV testing among high school students in the southern states were available in Texas (13.5%), Louisiana (22.5%), South Carolina (12.1%) and North Carolina (10.8%) while Mississippi, Alabama and Georgia did not have weighted data.[1]

Adolescents are one of the most challenging groups to engage in healthcare. They are disproportionately impacted by incidence of HIV infection. And yet, they are the least likely to be linked to healthcare in a timely fashion. They are also the least likely group to have viral suppression.[2] To optimize the care of adolescents and young adults impacted by HIV would entail the best of implementation science including innovative models of healthcare for this group. Short of bringing the clinic to the adolescent doorstep, this calls upon not only the infrastructure for innovative strategies but integrating adolescent healthcare services in rural and resource-limited communities.

School-Based Health Centers

CDC supports the implementation of effective interventions such as sexual health education, youth-friendly health services and safe, supportive environments. These all provides great resources for school-based health programs for adolescents. On top of this is the CDC's Youth HIV, STD, & Pregnancy Prevention Program that develops linkages between education and public health, delivers quality health education, creates systems to link students to health services and establishes safe and supportive school environments.[6] From 2015 to 2017, as a result of school-based programs, there was a significant decrease in youths' level of sexual risk behaviors.[6] From 2014 to 2018, CDC funded and implemented four key school connectedness programs (high risk substance use, mental health and suicide, sexual behavior and violence victimization) that impacted more than risky sexual behaviors.[6]

Another school-based program for adolescents is the Get Yourself Tested (GYT) which is a campaign empowering young people to get tested for HIV and STDs.[7] This is a joint program between the students and the school staff developing materials for school-wide activities concerning HIV and STD prevention and testing.[7] It is intended for both sexually active and non-sexually active youths regardless of their ethnicity, gender, race and sexual orientation.[7] The GYT campaign is intended to educate the youth on HIV and STDs as well as prevention, connecting adolescents to testing and counseling services and promoting open discussions with healthcare providers, peers and their partners.[7] Additional information is available online on how schools are in a unique position to support and encourage students to get tested for HIV.[8] (https://www.cdc.gov/healthyyouth/sexualbehaviors/pdf/hiv_testing_fact_sheet.pdf?s_cid=tw-zaza-1179)

All these school-based strategies and projects should be tailored towards the needs of the youth in rural areas and other resource-limited communities. While these programs are promising, most high school students do not have access to effective school-based interventions. In fact, CDC reaches less than ten percent of the more than 26 million high school students in the U.S.[6] Also most schools nationwide are not teaching the 11 key HIV, pregnancy and STD prevention topics as a required course in middle and high schools. Most schools do not have a student-led inclusive club and a majority do not provide on-site services or referrals to healthcare providers.[6]

ISTOCK/MONKEY BUSINESS IMAGES

All these school-based strategies and projects should be tailored towards the needs of the youth in rural areas and other resource-limited communities. While these programs are promising, most high school students do not have access to effective school-based interventions.

Table 1. Various comprehensive support system being provided in a one-stop shop clinics

(Adapted from RHIhub – Rural Health Information Hub, https://www.ruralhealthinfo.org/toolkits/hiv-aids/2/manage/one-stop-shop)

- Care coordination
- HIV testing
- Improved access to health insurance and healthcare
- Routine vaccination services
- Substance use disorder treatment referrals
- Transportation assistance for accessing healthcare services

Table 2. Various technology-based platforms in improving adherence and engagement to HIV care among YLWH

- Ability to directly message clinics and providers or real-time engagement to receive individualized counseling support
- An anonymous support group among YLWH through a private Facebook network that allows teens to share their adherence problems, lessen social isolation and provision for emotional social support
- Computer-delivered interventions for YLWH such as computer-based motivational interviewing intervention and a private telehealth or remote video-conferencing that includes medication adherence counseling
- Health educator using different social media platforms based on the YLWH preference
- Interactive daily text messages to improve adherence
- Personalized content of text messages and the use of animated memes or Graphics Interchange Formats (GIF)
- Personalized text message reminders

We should not undermine the participation and shared responsibility of parents, community leaders and teachers making a more impactful intervention for adolescents.

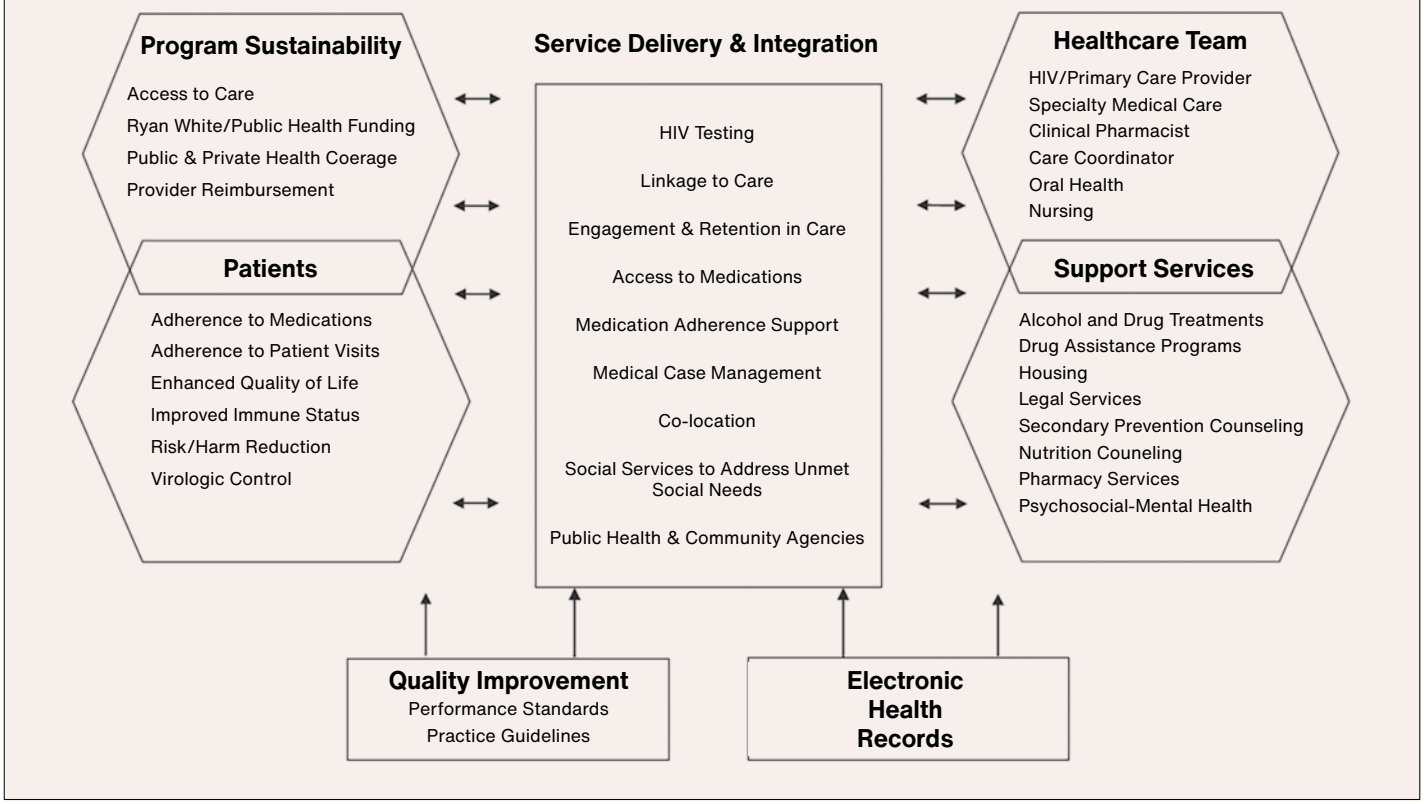
Mobile Clinics, Mobile Vans

Mobile clinics and mobile outreach projects may work for hard to reach communities, rural areas and resource-limited settings where transportation to the nearest clinic is a major barrier. A mobile outreach strategy for screening hepatitis C and HIV has proven to be effective in providing access for high-risk populations in several locations in western Massachusetts.[9] They identified two important priorities in the success of mobile outreach projects among inaccessible at-risk populations: effective educational resources for counseling and teaching.[9] The use of mobile vans has been instrumental in finding HIV positive youth. This outreach method may work for adolescents who remain a "hidden population" in our efforts to identify HIV infections and eventually link and engage them to care. Enhancing the visibility of mobile vans' on the street should be tailored to different geographic settings particularly in community locations, to increase acceptance and engagement among the youth.[10]

One-Stop Shop

In many rural programs or resource-limited communities, a one-stop shop model may be the most appropriate in providing comprehensive healthcare to youth living with HIV (YLWH).

Figure 3. Essential Components of a Comprehensive HIV Care Model



CLIN INFECT DIS. 2011 DEC;53(11):1043-50. DOI: 10.1093/CID/CIR689

The one-stop shop HIV/AIDS program provides an entire spectrum of services in both health and non-health related issues.[11] (Table 1) Provisions for many healthcare services are under one roof which can be effective in reducing challenges related to adherence and retention to HIV care.[11] The essential components of a comprehensive HIV care model have been identified in a public policy statement by the HIV Medicine Association.[12] (Figure 3) Furthermore, most one-stop shop clinics are tailored to address the needs and barriers of specific populations, which make them beneficial for YLWH.

A recently established multidisciplinary clinic for LGBTQ patients is now serving both the rural and urban communities around Jackson, Miss. Aptly named the TEAM (Trustworthy, Evidence-based, Affirming and Multidisciplinary Care) Clinic opened its doors last September 2019 not only for adults but also for adolescents.[13] It is a safe haven for young individuals who may not fit well in their local communities. It is situated in what used to be a mall and provides different medical and non-medical services under one roof tailoring to the specific needs of the LGBTQ population. The multitude of healthcare services includes primary care, gender affirmative medicine including hormone therapy, HIV/STD screening and treatment and behavioral health services including therapy and medication management. The University of Mississippi Medical Center is fully committed in maintaining diversity and supports the TEAM Clinic by providing medical staff: endocrinologists, family medicine and internal medicine providers, HIV specialists, pediatricians, psychiatrists as well as psychologists. As with other one-stop shop clinics, transportation remains a barrier for those living more than an hour away.

Technology-Based Interventions

There is growing evidence on the use and feasibility of technology-based interventions among teens and young adults in improving engagement and adherence to their HIV care. A recent survey from Pew Research Center – Internet & Technology reported nearly all teens and young adults (18 to 29 years old) own cell phones even in rural areas (95%).[14] This includes ownership of smartphones which remains high in both urban (83%) and in rural settings (71%).[14] A recent systematic review on electronic health (eHealth) and mobile health (mHealth) described the acceptability and feasibility of technology-based interventions in reducing disparities in the clinical outcomes related to adherence and viral suppression among YLWH.[15] The unique adherence patterns among YLWH and their increased use of cell phones makes the several technology-based strategies appealing as summarized in Table 2.[15] These interventions may overcome several structural barriers particularly in rural and resource-limited settings where clinic scheduling difficulties and transportation challenges are major issues.

We should have more information in the recently concluded

mixed-methods study consisting of a set of interrelated strategies to prevent and treat HIV infections in high-risk youth and YLWH in the U.S.[16] Rather than focusing on a particular app, the technology-based interventions used in this study are truly innovative i.e. off-the-shelf and rapidly deployable tools adaptable for flexible communication channels, private social media discussion forums and SMS text messaging.[16] The research was conducted in Los Angeles and New Orleans from May 2017 to June 2019.

Online Resources and Suggested Readings

There are several online resources available to medical providers from the American Academy of Pediatrics, that address some of the challenges and practical issues when caring for adolescents (https://pedialink.aap.org/visitor/home) and from other organizations.

"Affirming Medical Care for LGBTQ Adolescents" aimed to help clinicians in being consistent with the definition of LGBTQ and gender identity, to be inclusive in providing healthcare services to LGBTQ youth, identify risk factors confronting LGBTQ youth and applying current recommendations on STI screening for this vulnerable group of patients.

"Confidential Adolescent Care and Billing" designed to increase parental comfort with private time for adolescents with their providers, provisions for confidentiality protections in electronic medical record and various options for confidential services when billing is a concern.

"Let's Talk About Sex" intended to increase the number of medical providers who are comfortable in addressing the sexual health needs of adolescents as well as young adults.

Medicaid expansion and what it means for you from Healthcare.gov (https://www.healthcare.gov/medicaid-chip/medicaid-expansion-and-you/)

"Middle Childhood and Adolescence" designed to guide providers in the current preventive and health promotion needs of middle childhood and adolescents.

Recommendations for Electronic Health Record Use for Delivery of Adolescent Healthcare from the Society for Adolescent Health and Medicine. (https://www.ncbi.nlm.nih.gov/pubmed/24656534)

Towards a Progressive and Collaborative Future

I envision a future where integrated healthcare services are readily available for everyone, including those living in rural and resource-limited communities. I look forward to a progressive future where we set aside our differences and internal biases and work together towards the common goal of ending the HIV epidemic.[4] There should be a paradigm shift in our behavior as medical providers making HIV testing a routine part of every adolescent's clinic visit including in the emergency room or at an urgent care, to avoid missed opportunities. Implementation science holds great promise in the prevention and treatment of HIV infections and other STDs. However, we must tailor novel strategies to meet the needs in the local communities. Certainly, much needed funding should be secured and available to rural and resource-limited settings making the promise of innovative strategies operational. I hope for healthier, sexually-educated and empowered adolescents actively taking part in their healthcare and ready to transition to adulthood. **HIV**

ABOUT THE AUTHOR

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REFERENCES

1. Kann L, McManus T, Harris WA, et al. Youth Risk Behavior Surveillance - United States, 2017. *MMWR Surveill Summ* 2018; **67**(8): 1-114.
2. Centers for Disease Control and Prevention. HIV and Youth. 2019. https://www.cdc.gov/hiv/group/age/youth/ (accessed October 16, 2019.
3. Centers for Disease Control and Prevention. HIV Surveillance – Adolescents and Young Adults,. Atlanta, GA: National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention,; 2017. p. https://www.cdc.gov/hiv/pdf/library/slidesets/cdc-hiv-surveillance-adolescents-young-adults-2017.pdf.
4. U.S. Department of Health & Human Services. What is 'Ending the HIV Epidemic: A Plan for America'? 2019. https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview (accessed Oct 28, 2019.
5. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006; **55**(RR-14): 1-17; quiz CE1-4.
6. Centers for Disease Control and Prevention. CDC's Adolescent and School Health Program Protecting our Nation's Youth from HIV, STDs and Pregnancy. 2019. https://www.cdc.gov/healthyyouth/about/cdc-dash-health-program-impact.htm (accessed Oct 28, 2019.
7. Centers for Disease Control and Prevention. GYT: Get Yourself Tested for High Schools. https://www.cdc.gov/healthyyouth/get_yourself_tested/index.htm (accessed Oct 28, 2019.
8. Centers for Disease Control and Prevention. How Schools Can Support HIV Testing Among Adolescents2019. https://www.cdc.gov/healthyyouth/sexualbehaviors/pdf/hiv_testing_fact_sheet.pdf?s_cid=tw-zaza-1179 (accessed Oct 29, 2019).
9. Zucker DM, Choi J, Gallagher ER. Mobile outreach strategies for screening hepatitis and HIV in high-risk populations. *Public Health Nurs* 2012; **29**(1): 27-35.
10. Bell DN, Martinez J, Botwinick G, et al. Case finding for HIV-positive youth: a special type of hidden population. *J Adolesc Health* 2003; **33**(2 Suppl): 10-22.
11. Rural Health Information Hub. Rural Health Information Hub (RHIhub) - One-Stop Shop HIV/AIDS Program,. 2002-2019. https://www.ruralhealthinfo.org/toolkits/hiv-aids/2/manage/one-stop-shop (accessed Oct 15, 2019.
12. Gallant JE, Adimora AA, Carmichael JK, et al. Essential components of effective HIV care: a policy paper of the HIV Medicine Association of the Infectious Diseases Society of America and the Ryan White Medical Providers Coalition. *Clin Infect Dis* 2011; **53**(11): 1043-50.
13. R. C. UMMC opens primary care clinic for LGBTQ patients,. *News Stories*, October 10, 2019, 2019. https://www.umc.edu/news/News_Articles/2019/10/TEAM-Clinic.html (accessed October 31, 2019).
14. Pew Research Center. Internet & Technology. 2019. https://www.pewinternet.org/fact-sheet/mobile/.
15. Mulawa MI, LeGrand S, Hightow-Weidman LB. eHealth to Enhance Treatment Adherence Among Youth Living with HIV. *Curr HIV/AIDS Rep* 2018; **15**(4): 336-49.
16. Rotheram MJ, Fernandez MI, Lee SJ, et al. Strategies to Treat and Prevent HIV in the United States for Adolescents and Young Adults: Protocol for a Mixed-Methods Study. *JMIR Res Protoc* 2019; **8**(1): e10759.

Challenges Integrating Transgender Healthcare for Adolescents

Are They Living Their Best Lives?

BY MICHELLE COLLINS-OGLE, MD, FAAP, AAHIVS

BEAT-UP, BEAT-DOWN, bullied and using drugs to dull the pain, is how M.J. described her adolescent years as a transgender female. She began drinking alcohol at age 15 to cope with isolation and sometimes to "fit-in." Once M.J. "came-out" and began living life as a female, she was kicked out of her home and told to live any place where she could wear "girl clothes" and make-up. She certainly couldn't do it in her stepfather's house. According to M.J. and girls like her, it's an every day struggle to survive and live in their truths as females. M.J. says, "I don't go to the movies, hang out at the mall or have a favorite place to eat where everybody knows my name."

After leaving home, M.J. couch-surfed, dropped out of high school and after several months, engaged in commercial sex work to make money for food and rent, what she called "survival sex." "My life so far hasn't been that great, guess I need to make the next 20 years count because girls like me don't live that long." Above everything M.J. shared with me, those words were the most chilling and rendered me speechless. We'll come back to why this statement should give each of us pause.

M.J.'s first sexual experience was at age 16, initially having receptive anal intercourse with school-age boyfriends. As she became more experienced, exchanging sex for "favors" was the expectation from older male partners and this became a business transaction. She became concerned that she had a sexually transmitted disease (STD) but was too afraid to seek healthcare services. M.J. was ashamed and feared she was seen as "nasty" or deserving of an STD because she was a trans-teenage girl who was sexually active and homeless. M.J.'s grim outlook on life and mistrust of the healthcare system is not unique and is shared among most trans-youth of color. Trans-adolescents are among the most vulnerable youth and face the highest barriers when attempting to access comprehensive healthcare services.[1] M.J.'s journey, challenges and inability to access medical services without fear, including mental health, remains embedded within my soul and to a large extent, the reason I continue to advocate for the health and safety of transgender youth. We must forcefully demand the healthcare system improve access, engagement and retention of our most vulnerable youth into care.

I met M.J. at the age of 19 during her first hospitalization. I was consulted to see a patient with suspected Pneumocystis jirovecii pneumonia and a "weird-looking" rash. When I

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walked into her room we smiled and she immediately asked questions concerning her health. She was so eager to share her journey and tell me how she wound up hospitalized with pneumonia. After everything M.J. shared, I knew her life wasn't going to get any easier because I had to deliver the news she had syphilis and her HIV test was positive. The discussion began with connecting the rash to syphilis and pneumonia to HIV. Her nadir CD4 was 22/mm^3 and HIV viral load, 750,00 copies/mL. After hearing the words, "M.J., your HIV test is positive and you have AIDS," she said, "Okay, now what do we do?"

She is now 25-years-old and clinically doing well. M.J. is on a combination triple-antiretroviral drug regimen taken once daily. She struggles with adherence and depression, as do most adolescents and young adults with chronic diseases. As part of her comprehensive healthcare, M.J. is on a feminizing regimen consisting of injection estradiol valerate once every two weeks and oral spironolactone taken once daily. Adherence to medical appointments has improved as her body appearance has become more feminine. She feels more confident and admittedly happier. M.J. has achieved durable viral suppression and understands the importance of adherence to all medications if she wants to have a healthy, long life. Now back to M.J.'s comment, "Girls like me don't live that long."

Risks for HIV in Transgender Youth

The true prevalence and incidence of HIV in the transgender community is not accurately documented. The Centers for Disease Control and Prevention (CDC) estimates approximately 25 percent of transwomen living in the United States are living with HIV and about 50 percent of all transwomen diagnosed with HIV are black/African American.[2] Many transgender people living with HIV are unaware of their statuses and therefore, not included in statistics.

Trans-female youth and young men of color who have sex with men (MSM) of color, are disproportionally affected by HIV and experience disparities and barriers accessing healthcare. The following statistic is staggering: as much as 35 percent of trans-youth are bullied in school (Johns MMWR 2019).

According to the United States Transgender Survey in 2015:

- 29 percent of trans-youth live in poverty
- 47 percent face family rejection
- 14 percent experience homelessness
- 40 percent have attempted suicide; 10 percent attempted suicide within the last year
- 1 in 3 face discrimination in healthcare settings

HIV-related stigma is not the only form of discrimination this vulnerable population experiences. Other forms of stigma can result in an unpleasant and often fearful interaction between transgender adolescents and clinicians within the healthcare domain.[3] Transphobia is a major barrier for trans-youth to access healthcare, advanced education and employment. These structural barriers often lead trans-youth to engage in "survival sex" and substance misuse which are high risk factors for HIV acquisition as well as other STIs.

Too many trans-youth/gender non-binary (GNB) youth live in context of intersection discrimination.[3] That is, being transgender/GNB, poor, ethnic minority and homeless, which is multilayered and often unappreciated by clinicians and the healthcare system in general.

Importance of Providing Gender-Affirming Care

When it comes to engaging adolescents and young adults into care, it is important (if you want to have success) to understand that your priorities may not be their priorities. In M.J.'s case, after understanding what having AIDS meant, she wasn't very concerned about medication adherence and achieving a healthy immune system. I quickly understood that being a "real girl" was the most important thing in her life. If she couldn't be a girl, she didn't care about living. To improve adherence to ART and medical visits, together we created a medical plan that included gender-affirming care which included feminizing hormone therapy. It was important for her to understand if she wanted to be "Trans-Fabulous," she need to be "Trans-Undetectable."

Hormone therapy is an important part of comprehensive gender-affirming care. Concerns about interactions between ART and hormonal therapy is number one on the list of

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concerns for most transgender youth and should be the same for their healthcare providers.[4] Studies show increased nonadherence to ART in trans-females with HIV because they are concerned that ART will negatively interfere with hormonal therapy.[5] There is limited data on the pharmacodynamics of ART in people concurrently using feminizing or masculinizing hormones.[6]

Current literature citing data on drug interactions is primarily based on oral contraceptive use in cis-gender women or testosterone therapy for cis-men treated for hypogonadism.[6,7] Use of progesterone and spironolactone is often a component of hormone therapy in trans-people.

However, there is almost no data on the pharmacodynamics of these medications when used in trans-people on ART.[6,7] It is important for clinicians to emphasize that there are rarely contraindications to hormonal therapy. Providing hormonal therapy for trans-teens living with HIV has a powerful impact on engagement and retention into medical care. Clinicians providing care for adolescents and young adults with HIV should emphasize the connection between being healthy, maintaining durable viral suppression and living their best lives as they continue on their trans-journey. Clearly more research must be done and include teens and young adults to better understand hormonal therapy in the context of ART for trans-people living with HIV.

Violence Against Transwomen and GNB

In 2018, advocates reported at least 26 deaths of transgender or gender non-conforming people in the U.S. due to violence, the majority of whom were black, transgender women. The average age of the people murdered was 33 years. Oftentimes, these victims were killed by acquaintances, partners and strangers. Some of these cases were clearly associated with transphobia. In other cases, being a transgender female may have put them at increased risk of being victims of violence such as forcing them into unemployment, poverty, homelessness and survival sex work.

The statistics appear to be worse for 2019, which has already seen at least 22 transgender or gender non-conforming people fatally shot or killed by other violent means. Fatal violence against transgender women is frightening as the average age is considerably younger at 30. According to the Human Rights Campaign, it is important to note that many transwomen of color are murdered and these murders are never reported and go unsolved.

Back to M.J. and the fear she won't live that long. It shouldn't go unrecognized that these young transwomen of color are aware of the continued threat of violence against their communities and they too fear they may be next. M.J.'s fear of not living long has also become mine. When she misses an appointment or doesn't respond to a call, I fear the worst. This fear is now projected onto all of my transgirls. If they miss an appointment, I've instructed several of them who I know engage in survival sex to at least call and say, "I'm alive!" They know I'm concerned and need to know they are all right.

Addressing "The Talk" With a Transgender Child

M.J. described the most miserable childhood imaginable because "he" was born a boy, assigned male and grew up with brothers. M.J. vividly remembers the expectation to

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What can Clinicians do to Improve Comprehensive Care?

1. Provide compassionate healthcare in a non-stigmatizing, affirming environment
2. Make sure clinic staff and support personnel are knowledgeable, culturally sensitive and respectful. Not using the patient's "dead name" is germane.
3. Likewise, clinicians must demonstrate ongoing training and education to remain current in healthcare needs of transgender adolescents.
4. Educational materials designed to improve clinicians ability to provide evidence-based, high-quality care for transgender patients. The World Professional Association for Transgender Patients (WPATH) (https://www.wpath.org) provide guidelines for healthcare clinicians. Another excellent source for transgender clinicians is University of California, San Francisco (UCSF) Transgender Care & Treatment Guidelines. https://transhealth.ucsf.edu
5. Use preferred names and pronouns. Apologize to the patient when you make a mistake. Our patients are very forgiving and will accept an honest mistake.
6. Recognize and document trauma as well as PTSD in transgender adolescents. It is key to their overall health and may help in ongoing high-risk behaviors. Providing mental health services needs to be incorporated as part of comprehensive healthcare.

do all the things "boys" do and participate in sports with his older brothers. The more feminine M.J. tried to be, the harder everyday life as a boy became. When M.J. was 10-years-old, she visited the doctor for a school physical. M.J. tried to explain how difficult it was to feel like a girl on the inside, but looking like a boy on the outside. M.J. tried to tell the doctor that girls didn't seem to be attractive to him, and that he really liked boys. The doctor reassured M.J. that this was a phase and that some boys go through this phase.

These issues worsened for M.J. during middle-school sex-education class. Sex-education curricula does not include same gender sexual relationships, transgender or GNB. Current sex-education curricula is designed to encourage abstinence or delay sexual debut and prevent teenage pregnancy. STI prevention is only taught in the context of condom use in heterosexual vaginal sex. For LGBTQ pre-adolescents and adolescents, these conversations and school-based sessions are useless. Furthermore, it is

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More research is needed to understand any possible long term drug-drug interactions between hormone therapy and ARV. HIV research in transgender youth living with HIV has the potential to better inform the best treatment protocol for hormone therapy in this population.

reported that there is virtually no information or on-line resources to help parents navigate or negotiate conversations with their sons and daughters about same-gender sexual relationships.[8,9] For a transgender child like M.J., these years can be terribly challenging leading to depression and suicide attempts.

How do we Help Trans-Adolescents Live Their Best Lives?

Compared to any other age group, adolescents in general are least likely to be screened for HIV.[10] In the U.S., less than 10 percent of high school students have ever received a test for HIV and overall varies between 8 percent to 23 percent in states with available data.[11] Transgender adolescents of color must also be an integral part of HIV testing and prevention as their engagement is a critical component of "Ending the HIV Epidemic (EtHE)." Trans-youth must be able to access healthcare in a non-stigmatizing, gender-affirming environment with culturally-competent clinicians. Too often transgender adolescents of color have a negative experience when attempting to access healthcare services. Stigma, transphobia and structural racism negatively impact engagement and retention into medical care.

As we look forward, it is imperative that we examine ways to eliminate these barriers and find facilitators to encourage and welcome vulnerable LGBTQ into the healthcare system. The goal must be to engage them in care before exposure to HIV or before they become infected with other STIs.

Transgender adolescents of color disproportionately experience discrimination in a variety of ways: within the healthcare system, within their families, within the education system and within the employment sector. Discrimination and insensitivity in healthcare is common, causing most transgender people to delay or avoid obtaining medical care altogether.

Negative experiences ranges from disrespect and harassment to culturally non-inclusive clinics and flat out denial of medical treatment. Discrimination and insensitivity, combined with lack of knowledge about the healthcare needs of transgender and GNB youth, provide a powerful deterrence from obtaining care.

An equally important yet not well discussed challenge for the future is the need to include transgender adolescents and young adults living with HIV in research.[1] Overall, transgender and GNB people are disproportionally impacted by HIV, and yet, not well represented in HIV research.[1] More research is needed to understand any possible long term drug-drug interactions between hormone therapy and ARV. HIV research in transgender youth living with HIV has the potential to better inform the best treatment protocol for hormone therapy in this population.

Finally, creating initiatives to provide support services for transgender youth can help decrease high-risk situations like survival sex. Gilead has been pivotal in this endeavor. In 2017, one company pledged $100 million over 10 years to address stigma and disparities in the south. The TRANScend Community Impact fund was established to improve the lives of transgender people. This initiative originated from an advisory panel composed of transgender people and organizations that provide services for people of trans-experience.

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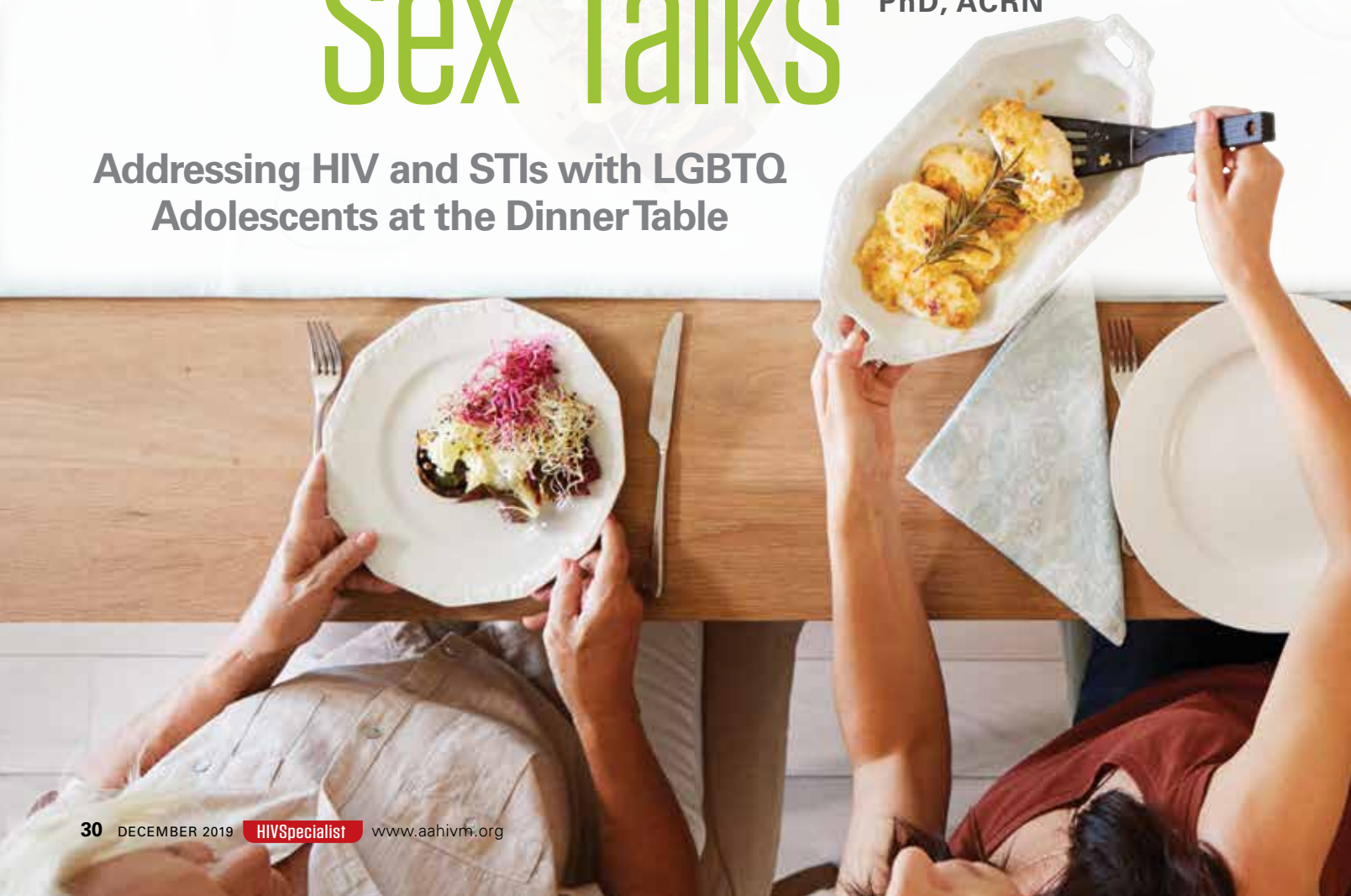
REFERENCES

1. Baral SD, Poteat T, Stromdahl S, Wirtz AL, Guadamuz TE, Beyer C. Worldwide burden of HIV in transgender women: A systematic review and meta-analysis. Lancet Infect Dis 2013: 13.214-22.
2. Centers for Disease Control and Prevention. HIV among transgender people. Atlanta, GA. CDC 2014.
3. Reisner SL, Hughto JM, Dunham EE, et al. Legal Protections in Public Accomodations Settings. A Critical Public Health Issue for Transgender and Gender-Nonconforming People. The Milbank quarterly. 2015:93(3):484-515.
4. Hembree WC, Cohen-Kettenis PT, Gooren I, et al. Endocrine treatment of gender-dysphoric / gender-incongruent persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2017; 102: 3869-903.
5. Braun HM, Candelario J, Hanlon CL, et al. Transgender women living with HIV frequently take antiretroviral therapy and/or feminizing hormone therapy differently than prescribed due to drug-drug interaction concerns. LGBT Health. 2017;4(5):371-375.
6. Blick G, et al. Testosterone replacement therapy in men with hypogonadism and HIV/AIDS: results from the TRiUS registry. Postgrad Med. 2013 Mar;125(2):19-29.
7. Radix A, §, Sevelius J, Deutsch MB. Transgender women, hormonal therapy and HIV treatment: a comprehensive review of the literature and recommendations for best practices. J Int AIDS Soc. 2016. (19:20810).
8. Flores D, et al. ""It's Almost Like Gay Sex Doesn't Exist": Parent-Child Sex Communication According to Gay, Bisexual, and Queer Male Adolescents." Journal of Adolescent Research 34.5 (2019): 528-562.
9. Flores D, Abboud S, Barroso J. "Hegemonic Masculinity During Parent-Child Sex Communication with Sexual Minority Male Adolescents." American Journal of Sexuality Education (2019). http://dx.doi.org/10.1080/15546128.2019.1626312
10. Centers for Disease Control and Prevention. HIV and Youth. 2019. https://www.cdc.gov/hiv/group/age/youth/ (accessed October 16, 2019).
11. Kann L, McManus T, Harris WA, et al. Youth Risk Behavior Surveillance - United States, 2017. *MMWR Surveill Summ* 2018; **67**(8): 1-114.
12. U.S. Department of Health & Human Services. What is 'Ending the HIV Epidemic: A Plan for America'? 2019. https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview (accessed Oct 28, 2019).

Not Your Parents' Sex Talks

BY DALMACIO FLORES, PhD, ACRN

Addressing HIV and STIs with LGBTQ Adolescents at the Dinner Table



EXCERPT 1: *I have to preface this by saying that talking to your kids about sex is really, really icky. So, John, my bisexual teen son, came into my bedroom, and wanted to know if he could get an STD from kissing. I had to try not to laugh because when you hear a question like that you just kind of want to die. So he was sixteen and I was like, "No, you can't get STDs from kissing, but you can catch colds or strep throat or the flu, or something like that." And I said, "You have to have sexual contact to catch an STD. So as long as you're not having sexual contact involving anything under the pants, you're not going to catch an STD." And he's like, "Oh, OK, whew." And I said, "Any time that contact is involving anything under your clothes, under your pants, you need to use a condom so you don't catch an STD. So, mouth to under-the-pants contact, you need to take precautions." Knowing his sexual orientation, I don't know if he's going to be with a man or a woman, so that "under the pants" kind of was my way of saying, "whomever you're with," whether you're with someone who's trans, or male or female… or intersex. It's just so awkward. I can talk with my coworkers about these things. It's not embarrassing to say penis, but with my kid, I just wanna die.*

—Linda, mother of a bisexual son

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While Linda's story may seem commonplace and resonate with parents with heterosexual teenagers, her situation is unique in that she does not have any personal experience or insight on how it is to come of age as a lesbian, gay, bisexual, transgender or queer (LGBTQ) adolescent. Most heterosexual parents use their own experiences, including their own parents' missteps, as a guide for having discussions about sex and health with their children at home.[1] Aside from the challenge of trying to come up with accurate responses to children's sex-related questions, for many parents, making LGBTQ sexual health a central consideration in home-based sex talks is unchartered territory.

Adolescent LGBTQ Health Disparities

Societal acceptance of LGBTQ individuals in the U.S. is on the rise, which may account for earlier ages of sexual and gender minority teens coming out. Despite these positive trends, LGBTQ youth still have disproportionate rates of negative health outcomes compared to their heterosexual counterparts. For example, not only are young men who have sex with men still more at risk for contracting HIV/STIs compared to other youth groups,[2] they also report greater dating violence and forced sex.[3] Compared to their cisgender counterparts, not only are transgender youth more likely to experience violence victimization, substance use and suicide risk[4] but overall, 9 percent of transgender people are HIV-positive, while HIV prevalence among U.S. cisgender adults is less than one percent.[5]

When compared to their heterosexual female peers, LBQ female adolescents engage in more frequent sexual relations. According to data from the most recent Youth Risk Behavior Surveillance Survey of U.S. high school students, only 25 percent of lesbian-identifying youth and 27 percent of bisexual-identifying youth reported **never** having sex compared to 50 percent of heterosexual female youth.[6] For parents of LGBTQ youth, understanding sexuality-sensitive, parent-child sex communication can help them meet their child's needs.[7] To date, parental guidance for information-seeking and skill-building as a strategy to deter these negative health outcomes for emerging LGBTQ youth has been largely understudied.[8,9]

Hegemonic Masculinity and Inclusive Parent-Child Sex Communication

Consistent and effective sex talks, the bi-directional discussions between parents and their children about sex and health-related topics, at home are associated with condom use, delayed sexual debut, teens' capacity to broach HIV prevention with sexual partners and access and use of reproductive and sexual health services.[10-13] However, to date, no evidence-based sex communication intervention for families with LGBTQ adolescents has been published.

What we do know though from parents and GBQ sons is that both parties typically find sex discussions at home to be awkward and embarrassing[14] and that parents tend to provide heteronormative guidance with fathers placing a premium on making sure their sons are socialized into becoming heterosexual.[15,16] Additionally, Rose and colleagues[17] reported that parents found limited online information for YMSM's health which deterred parents from broaching sexual health talks with their sons. The experiences of families with cisgender LBQ adolescents and with transgender children are even more underreported.

Gay, bisexual and cisgender males have identified parents and healthcare providers as their preferred sources of sexuality-related information when they were younger.[18,19] Prior to leaving home for college or work, a sample of 30 GBQ adolescent and young adult males indicated that parents, in particular, would have been their preferred sexuality educators because they could anticipate questions based on pubertal milestones, provide answers on youth's emergent concerns, and engage with them in follow-up discussions throughout adolescence. Since the ecological systems outside the home is marked by hegemonic masculinity that makes it difficult for LGBTQ children to explore their unique attractions and identities (e.g. most school settings do not provide LGBTQ-specific sex education, peers are unreliable sources of sex information and can be sources of bullying), parents can be reconfigured as a proximal source of inclusive sex information. Preliminary data from our ongoing work with parents of GBQ cisgender males describes a parent group cognizant of the need to learn more about LGBTQ-specific health information and ways they can facilitate their sons' socialization as young men who will have sex with men.

In order to address the informational gaps in parents' knowledge, healthcare providers can be parents' allies as they step up to this new parenting charge. Just as important, healthcare providers can be parents' crucial resource for information about biomedical HIV/STI prevention options tailored around LGBTQ adolescents' behavior and risk profiles.

EXCERPT 2: ***It would be great to give parents information to assist their children with the decision to get preexposure prophylaxis or to help them make the decision about HPV vaccine, and so on. Protecting your son from diseases is important especially when it is within our means today.***

—Dori, mother of gay son

Providers Bridging Gaps

Healthcare providers are in a unique position to address the HIV/STI prevention needs of LGBTQ youth and in clarifying for parents the roles they can plan to mitigate these health risks. Aside from not assuming adolescents as heterosexual or cisgender during wellness visits, providers can normalize with parents and youth the sexual and gender fluidity that is a hallmark of adolescence. Aside from having visible signage to indicate that one's practice is a safe space for LGBTQ individuals (e.g. having rainbow stickers or inclusive mission statements prominently displayed in waiting rooms), providers can model how to have nonjudgmental discussions about sexual behavior for parents and youth and how to search online from credible health sources.

Given the common parental fear that talking about sex with children leads to sexual experimentation or early sexual debut, providers can cite recent studies that have debunked such beliefs (e.g. Widman et al, 2019) and make explicit the established outcomes related to consistent and open sexual health discussions (e.g. condom use, comfort talking about sex). Regardless of a child's age, providers can also inquire if parents have started having routine sex talks at home, normalize for them the initial awkwardness of such conversations, identify and address barriers parents may have about this area of family discussion, and refer families to services that meet their unique circumstance. Local chapters of PFLAG (formerly Parents and Family of Lesbians and Gays) offer support groups for families whose child has just recently disclosed as LGBTQ.

Given the myriad of ways that unconscious bias detrimentally impacts how teenage LGBTQ patients and their families engage with the healthcare setting,[20,21] providers are cautioned against subsuming the experiences of patients and families from racial/ethnic backgrounds with that of gay, cisgender white men's experiences. Discrimination in the healthcare setting is a noted barrier that keeps racial/ethnic and sexual and gender minority individuals from staying engaged in care,[22,23] including preventive services.

Through an inclusive practice that acknowledges and balances an LGBTQ teen's growing sense of autonomy and parents' roles as caregivers, providers can partner with them to identify emergent sexuality questions or concerns. For example, with pre-exposure prophylaxis (PrEP) use among

adolescents approved by the FDA since 2018, providers can be the crucial resource that introduces this biomedical option to parents for an adolescent population that might maximally benefit from it. Parents' supportive roles (e.g. as adherence, emotional, financial or transportation support)[24] in the successful uptake of biomedical interventions such as PrEP for LGBTQ adolescents of color promises to be a robust area healthcare providers can make a difference in, especially given historical mistrust.

EXCERPT 3: ***Doctors of adolescents also need to recognize that parents should leave the room for part of the check-up. My kids' pediatricians were very good, but it wasn't until my son was 17 that one of them asked me to leave for a few minutes and had a conversation centered around whether he had a girlfriend and whether they were sexually active…I'm reasonably certain that there was no open-ended question about my son's sexual orientation. In retrospect, this seems to be something doctors of young people should find a way to address with their young patients in an accepting and confidential way.***

—Sarah, mother with a gay son

Future Work

Overall, providers can take the lead in dismantling heteronormative assumptions that reinforce sexual and gender binaries and show parents the many opportunities they have in ensuring their LGBTQ children's wellbeing. Parents we have worked with through the years want to be more involved in keeping their LGBTQ children healthy.

Our recently concluded study Parents Advancing Supportive and Sexuality-Inclusive Sex Talks (ASSIST),[25] a video-based pilot study that aimed to increase the amount of parents' LGBTQ health information and model inclusive communication skills when discussing sexual health with gay, bisexual and queer cisgender males, had very promising results. Our online study was able to recruit more participants than we initially targeted. Parents deemed the animated videos as an acceptable means of learning about LGBTQ content and inclusive sex communication, and clamored for more information beyond the roster of topics covered in our videos (e.g. HIV testing, PrEP access, condom and lube compatibility, etc.).

The Parents ASSIST pilot findings highlight the partnerships parents and providers can forge in covering all the bases crucial for ensuring sexual minority males' sexual health. They can serve as a basis for work with families who have female sexual minority and transgender adolescents. This nascent field of inclusive sex communication needs all hands on deck and can extend healthcare practice and patient and family education beyond traditional talking points. HIV

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REFERENCES

1. Flores, D.D & Barroso, J. (2017). 21st Century Parent-Child Sex Communication in the U.S.: A Process Review. Annual Journal of Sex Research. (54):532-548. Doi: 10.1080/00224499.2016.1267693. PMCID: 28059568.
2. Centers for Disease Control and Prevention (2018 Sept). HIV and gay and bisexual men [webpage]. Retrieved from https://www.cdc.gov/hiv/group/msm/. Retrieved June 21, 2019.
3. Centers for Disease Control and Prevention (2017). HIV Surveillance Report, 2017; vol. 29. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Retrieved July 14, 2019.
4. Johns MM, Lowry R, Andrzejewski J, et al. Transgender identity and experiences of violence victimization, substance use, suicide risk, and sexual risk behaviors among high school students—19 states and large urban school districts, 2017. Morb Mortal Weekly Rep. 2019;68(3):67.
5. Centers for Disease Control and Prevention. HIV and transgender communities. . 2019. https://www.cdc.gov/hiv/pdf/policies/cdc-hiv-transgender-brief.pdf.
6. Rasberry CN, Lowry R, Johns M, et al. Sexual risk behavior differences among sexual minority high school Students—United states, 2015 and 2017. Morb Mortal Weekly Rep. 2018;67(36):1007
7. [7] Tortolero, Susan R. "Innovations in adolescent health: New approaches to sexual minority youth research." (2010): 259-260.
8. Newcomb ME, LaSala MC, Bouris A, et al. The influence of families on LGBTQ youth health: A call to action for innovation in research and intervention development. LGBT Health. 2019;6(4):139-145. doi: 10.1089/lgbt.2018.0157.
9. Harper GW, Riplinger AJ. HIV prevention interventions for adolescents and young adults: What about the needs of gay and bisexual males? AIDS and Behavior. 2013;17(3):1082-1095.
10. Hadley W, Brown LK, Lescano CM, et al. Parent–adolescent sexual communication: Associations of condom use with condom discussions. AIDS and Behavior. 2009;13(5):997-1004.
11. Hall KS, Moreau C, Trussell J. Associations between sexual and reproductive health communication and health service use among US adolescent women. Perspectives on sexual and reproductive health. 2012;44(1):6-12.
12. Crosby RA, Hanson A, Rager K. The protective value of parental sex education: A clinic-based exploratory study of adolescent females. J Pediatr Adolesc Gynecol. 2009;22(3):189-192.
13. Widman L, Evans R, Javidi H, Choukas-Bradley S. Assessment of parent-based interventions for adolescent sexual health: A systematic review and meta-analysis. JAMA pediatrics. 2019;173(9):866-877.
14. LaSala, Michael C. "Condoms and connection: Parents, gay and bisexual youth, and HIV risk." Journal of marital and family therapy 41.4 (2015): 451-464.
15. Flores, D., Abboud, S. and Barroso, J. "Hegemonic Masculinity During Parent-Child Sex Communication with Sexual Minority Male Adolescents." American Journal of Sexuality Education (2019). http://dx.doi.org/10.1080/15546128.2019.1626312
16. Solebello, N., & Elliott, S. (2011). "We Want Them to Be as Heterosexual as Possible": Fathers Talk about Their Teen Children's Sexuality. Gender & Society, 25(3), 293-315. doi:10.1177/0891243211403926
17. Rose, India D., et al. "Health communication practices among parents and sexual minority youth." Journal of LGBT Youth 11.3 (2014): 316-335.
18. Voisin, Dexter R., et al. ""It's crazy being a Black, gay youth." Getting information about HIV prevention: A pilot study." Journal of Adolescence 36.1 (2013): 111-119.
19. Flores, Dalmacio, et al. ""It's Almost Like Gay Sex Doesn't Exist": Parent-Child Sex Communication According to Gay, Bisexual, and Queer Male Adolescents." Journal of Adolescent Research 34.5 (2019): 528-562.
20. Calo, W. A., Cubillos, L., Breen, J., Hall, M., Rojas, K. F., Mooneyham, R., ... & Garcia, N. (2015). Experiences of Latinos with limited English proficiency with patient registration systems and their interactions with clinic front office staff: an exploratory study to inform community-based translational research in North Carolina. BMC health services research, 15(1), 570.
21. Macapagal, K., Bhatia, R., & Greene, G. J. (2016). Differences in healthcare access, use, and experiences within a community sample of racially diverse lesbian, gay, bisexual, transgender, and questioning emerging adults. LGBT health, 3(6), 434-442.
22. Hawley, S. T., & Morris, A. M. (2017). Cultural challenges to engaging patients in shared decision making. Patient education and counseling, 100(1), 18-24.
23. Tan, J. Y., Xu, L. J., Lopez, F. Y., Jia, J. L., Pho, M. T., Kim, K. E., & Chin, M. H. (2016). Shared decision making among clinicians and Asian American and Pacific Islander sexual and gender minorities: An intersectional approach to address a critical care gap. LGBT health, 3(5), 327-334.
24. Wood, S., Dowshen, N., Bauermeister, J. A., Lalley-Chareczko, L., Franklin, J., Petsis, D., ... & Gross, R. (2019). Social Support Networks Among Young Men and Transgender Women of Color Receiving HIV Pre-Exposure Prophylaxis. *Journal of Adolescent Health*. (Online ahead of print) Doi: 10.1016/j.jadohealth.2019.08.014.
25. Flores, D.D., Bond, K., Rosario, A., Villarruel, A., & Bauermeister, J. Parents ASSIST (Advancing Supportive and Sexuality-Inclusive Sex Talks): Iterative Development of a Sex Communication Video Series for Parents of Gay, Bisexual, and Queer Male Adolescents. *Journal of Family Nursing* (*in press*).

BY ACE ROBINSON, MHL, MPH

Adapting the Clinical Response to be Culturally Responsive

Achieving the Tenets of the EtHE Requires Partnership with Patients and not Stewardship

FOR NEARLY FORTY YEARS, the world has been aware of HIV. HIV has decimated not just the lives of individuals, but has destroyed entire communities, and has come close to functionally eliminating entire countries. For all of us living near the end of the millennium, HIV is and remains the epidemic of our lifetimes. Thanks to tireless clinicians, researchers, patients, supporters, and advocates, new and better treatments were created that not only extended life, but additionally improved the quality of life for people living with HIV (PLHIV) and indirectly for those people who support them. HIV best clinical practices have been dynamic with steady updates to ensure that PLHIV have improved health outcomes. This is a result of patient-driven advocacy and clinical researchers who have not only focused on the biological needs of people impacted by the virus, but also on their sociopolitical needs.

The HIV response required a high level of coordination in order to reach the point where it is today. That coordination goes beyond care coordination amongst primary care and infectious disease clinicians. It has required political will, community engagement and expanded access to HIV prevention and treatment options in addition to optimal clinical care. In February 2019 at the State of the Union address, President Donald J. Trump announced a new federal initiative to End the HIV Epidemic (EtHE) by 2030. The goals were simple: 1) *diagnose* all PLHIV; 2) *treat* PLHIV rapidly and effectively to reach sustained viral suppression; 3) *prevent* HIV with proven interventions, i.e. pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs); and 4) *respond* quickly to potential HIV outbreaks. However, execution of EtHE will not be simple.

EtHE focuses on the 57 most HIV-impacted jurisdictions (cities, counties, states) in the United States and its territories where the majority of PLHIV reside. In some of these jurisdictions, the HIV response has been suboptimal with the impact of the virus still expanding. In other areas, the HIV response has been robust which has led to successful reductions in HIV incidence and HIV-related deaths for much of their communities. However, across all jurisdictions, any level of success has been uneven with key subpopulations being disproportionately impacted by HIV, i.e. Black/Latinx/American Indian GBTQ+ individuals, Black cisgender heterosexual women, people living with substance use disorders (SUDs), and those experiencing homelessness and/or transitionally housed.

Through EtHE activities in the identified jurisdictions, a concerted effort is being launched to help PLHIV and those at-risk for HIV acquisition to access clinical care. However, accessing clinical care and treatment will not be enough. Those individuals will need to stay in care. Until a cure is found, PLHIV will need to stay in care for the rest of their lives and people at-risk of HIV acquisition will need to stay in care through their identified *seasons-of-risk*. Through a plethora of clinical care data, we know that the patients' experiences with the medical system before and during medical care greatly impacts their desires to seek care initially and to also begin and adhere to treatment/prevention plans. Medical mistrust in clinical care goes well beyond HIV, especially in the highly impacted subpopulations. Changing this phenomenon will be at the core to end the HIV epidemic in the United States. Success will be rooted in one thing and one thing only: true partnership between healthcare providers and their respective patients.

For many patients, trust will need to be earned and not assumed which may require some clinicians to amend their bedside manners and address any explicit or implicit biases that they may harbor. Like in any relationship, true partnership requires open and honest communication that can only be accomplished through nonjudgmental culturally-responsive engagement devoid of prejudice. The patients must feel comfortable sharing their lived experiences to their clinicians which includes sexual and reproductive histories in addition to substance use histories, familial/friend support and current living situations.

To foster open and honest communication, healthcare providers and their support staff must facilitate an environment throughout the clinical space where each patient feels honored and valued. For instance, clinical staff, not

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just the providers, need to be culturally responsive to the needs of transgender/gender non-conforming people (T/GNC). T/GNC individuals, especially Black and Latinx identified people, experience extremely high rates of HIV acquisition and HIV-related mortality. This is exacerbated by the poor clinical experiences that many T/GNC people encounter when they do seek care from being misgendered by staff; not being able to access gender-affirming public accommodation, i.e. restrooms; and even being denied or delayed treatment for gender-affirming care and/or HIV prevention or treatment.

Success will be rooted in one thing and one thing only: true partnership between healthcare providers and their respective patients.

Many PLHIV have been diagnosed late. They have engaged healthcare multiple times prior to their initial diagnoses either in primary care or emergency room settings. Missed opportunities can be traced to a clinical assessment that the person is not at-risk for HIV infection or due to clinical discomfort with taking a full sexual/drug history of the patient. The first step to accessing treatment is diagnosis. And once diagnosed, best clinical practices states that the person should initiative treatment immediately. Clinical bias has unfortunately led to a delay in treatment post-diagnosis, especially for Black/Latinx/American Indian GTBQ+ individuals, Black cisgender heterosexual women, people living with substance use disorders and those experiencing homelessness. Clinicians often hold the key to the initial gateway to treatment. And when that key is withheld, those individuals and those that they love are impacted.

Patients may be unaware of the expansive benefits of initiating and staying on treatment. Not only does a person on sustained successful treatment mitigate the impact of HIV through viral suppression, the person also eliminates any chance of passing the virus onto a sexual partner. In a world filled with HIV-related stigma and fear of PLHIV, the message that Undetectable equals Untransmittable, or U=U, needs to be relayed. Far too many patients report and clinicians self-report that U=U education is withheld in clinical settings to the detriment of PLHIV. One internationally renown advocate, William Matovu, repeatedly states that the HIV-impacted community cannot tolerate *HIV Colonialism* where the clinical gatekeepers decide whom has access to life-sustaining treatment and whom is educated about U=U.

Nowhere is the success of the EtHE initiative more dependent on clinicians than in the offer and utilization of Truvada® or Descovy® as PrEP at-risk for HIV acquisition. The messaging and offering of PrEP are often completely reliant on clinicians since the vast majority of people are unaware that PrEP even exists. PrEP is over 99 percent effective at averting sexual acquisition of HIV when taken as prescribed. And for receptive partners solely practicing anal sex and insertive partners, intermittent PrEP has proven to be just about as effective when following the 2-1-1 dosing scheme. Only through effective communication and partnership between the patient and the clinician can an HIV-prevention strategy be optimally obtained.

In the world of PrEP, post-exposure prophylaxis (PEP) and U=U, clinicians can guide patients to make safer sex choices. These choices may or may not include the utilization of condoms which previously were the only option to greatly decrease the possibility of sexually passing/acquiring HIV when one partner is living with the virus. Now, that has changed. Clinicians have the opportunity to partner with their clientele to live healthier lives. Thirty-eight years since the identification and pathology of HIV has taught one thing: clinical and community messaging based in fear, abstinence and prejudice has not and will not get aid in the collective goal to end HIV. HIV

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Adolescents and the Fear of Addressing Substance Use and Addiction

BY MICHELLE COLLINS-OGLE, MD, FAAP, AAHIVS

ADOLESCENT DRUG ADDICTION AND SUBSTANCE ABUSE PROBLEMS are one of the most serious crisis among youth in America.[1] Adolescent substance use is often complicated by fear and denial. Confronting substance use in the adolescent patient can be frightening, in part, because neither the parent nor child wants to admit there could be a serious problem. Denial is an intellectual act by which people dismiss or block the evidence of an experience: the existence of a painful past, of a current traumatic event, or of a fear of potential danger that may have a negative impact.[2]

As substance use becomes more serious, denial gets more powerful with the young person stubbornly refusing to acknowledge the need for help, as the effects of substance use are altering their life. Initially, the parent may deny their child has a problem. The adolescent denies they are behaving differently and the clinician may underestimate drug use and denies that their patient may be struggling with addiction. In today's environment, adolescent substance use and misuse is more of a serious challenge than at any time in recent history.[3] Addiction occurs when repeated use of drugs changes how a person's brain functions over time. The transition from voluntary or "recreational" to compulsive drug use reflects changes in the brain's natural inhibition and reward centers that keep a person from exerting control over the impulse to use drugs - even when there are negative consequences.[3] This is the defining hallmark of addiction.

Clinicians have a unique position in dealing with substance use as it relates to the the pediatric patient population. Children and adolescents may have incidental exposure to illicit substances or knowingly take them. The current opioid crisis, has components of a pediatric problem as well. Thousands of babies are born yearly with opioid withdrawal symptoms and management of neonatal abstinence syndrome is often done by the pediatrician or neonatologist. Frequently, pre-schoolers and young children have accidental ingestion of adult caregivers' pain medications, prevention and treatment of these unintentional exposures are managed by the pediatrician or emergency room personnel. Children and adolescents are being prescribed opioids for too long and in doses that are too high for their body weight.[4] Identification of youth at high risk for substance use disorder (SUD) is germane and can be very challenging for pediatric and adolescent clinicians. There are many risk factors, including genetic vulnerability, prenatal exposure to alcohol or other drugs, lack of parental supervision or monitoring, and association with drug-using peers all play an important role.

Adolescents and young adults are struggling with substance use disorder (SUD) and addiction at alarming rates.[5] Pediatricians and other Primary Care providers are on the front lines and likely to engage with a child at any age who has

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been accidently exposed to illicit substances or is struggling with issue related to addiction. Despite its pervasiveness, addiction to opioids as well as other illicit substance use may elude the clinicians. No matter how disruptive their lives have become, youth who regularly use and rely on substances to function do not usually self-refer for help. Youth addiction is prevalent in today's society, which often leaves parents feeling powerless, helpless and not in control.

The Problem of Adolescent Drug Addiction

Many adolescents consider experimenting with drugs and alcohol to be a normal part of growing up. Teenagers are often exposed to street drugs upon entering high school. The four-year period between entering high school and graduation are important formative years and often transformational. It's also a time to experiment, and for millions of youth, this may mean trying alcohol and drugs. The availability of drugs at school is surprisingly high. Schools have taken a strong stance on illicit drug and alcohol use, however even with their efforts, addiction and SUD are still on the rise.[5]

There are various types of drugs that are available to high school students. SUD has a major impact on school performance in children and adolescents. Grades often suffer due to lack of energy and focus, poor concentration, and loss of personal drive. Students using alcohol or drugs often lose interest in extracurricular activities and other social organizations. Ultimately if not addressed, SUD and addiction can lead to not only academic failure, but to the student dropping out of school all together. Sadly, some teens using drugs will suffer more serious consequences as a result of their substance use.

Many developmental changes occur during the adolescent years, including physical, psychological and behavioral changes. Adolescence can be a time for experimentation, testing boundaries, rebellion and poor choices. Some of the problems young people face stem from these characteristics, as they lead to curiosity and identity formation. Some adolescents may use drugs and alcohol in response to peer pressure or out of a desire to fit in and form personal bonds. Other adolescents may start to use out of curiosity or boredom, while other adolescents may use drugs and alcohol as a way to cope with low self-esteem, depression and stress. Some children and adolescents are introduced to drug use through prescriptions and then gradually begin to use recreationally. Some youth begin experimenting with drugs as a result of friends or become curious after watching a movie or video referencing drug use. Some discover drugs by stealing from their parents' medicine cabinets. No matter how a child or adolescent first begins using drugs, prescription medications or drinks alcohol, addiction is a very real risk. Students have high rates of drug use, in fact 1 out of 5 students admit to use of drugs. Commonly used drugs by students in 2017 survey (Used in the past 30 days): [6,7]

Drug	Among 12th Graders	Among 10th Graders	Among 9th Graders
Alcohol	61.5%	42.2%	23.1%
Marijuana	45%	37%	13.5%
Adderall	5.5%	4%	1.3%
Inhalants	4.9%	6.1%	8.9%
Amphetamines	9.2%	8.2%	5.7%

The most striking realization is how much alcohol and marijuana is used in the lower grades. Almost as troubling is how easily-available these drugs truly are.

We can't overlook the fact that many adults and adolescents may use drugs or drink alcohol and it never lead to addiction. There are people who are more vulnerable to addiction than others, due to a range of possible factors including genetic. Stressful early childhood experiences such as being abused or suffering other forms of trauma are one important risk factors.[8] Adolescents with a history of physical and/or sexual abuse are more likely to be diagnosed with SUD or addiction.

As we approach 2020, clinicians who provide care for children, adolescents and young adults need to be aware that these young people face challenges that did not exist a generation or two ago. For parents, it is not enough to just keep an eye on their children or monitor social media use. Parents should have open dialogue with their children and adolescents regarding the dangers of drug and alcohol abuse. While education often starts at home, pediatric and adolescent clinicians must offer drug education information to teach them about the dangers of drugs and alcohol.

Clinicians who care for children and adolescents should pursue education about drug threats that were less prevalent a generation or more ago. Pediatric and adolescent clinicians must also overcome the fear of addressing SUD in children perceived as too young or "not that kind of kid." Some of the fear is based on the stigma associated with SUD. As clinicians, we must resist the fear of addressing SUD and addiction in young children. We must impart the message to our patients that substance use and misuse is **NOT** an inevitable "rite of passage" to adulthood. Even experimentation or casual recreational usage can quickly progress to dependence, abuse, and addiction. There are serious, even fatal consequences to substance use and addiction:

- Auto Accidents – **7-fold increased risk** to be in an alcohol-related car crash.
- Sexual Assault – **89%** of victims self-report drinking prior to the assault.
- Violence – Roughly **half of both assailants and victims** admit to using alcohol or drugs before the incident.

Stigma and Substance Use Disorder

Substance use disorders consistently rank among the most stigmatized conditions worldwide. Thus, this can make the

Some adolescents may use drugs and alcohol in response to peer pressure or out of a desire to fit in and form personal bonds. Other adolescents may start to use out of curiosity or boredom, while other adolescents may use drugs and alcohol as a way to cope with low self-esteem, depression and stress.

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conversation very challenging between the clinician and the pediatric patient. SUD stigma fosters health inequities among children, adolescents and young adults with substance use disorders and remains a key barrier to successful screening and treatment efforts. The Substance Abuse and Mental Health Services Administration's (SAMHSA) National Survey on Substance Abuse and Health states that while 21 million Americans aged 12 and over needed drug or alcohol treatment in 2016, only 3.8 million received the help they needed at a specialized treatment facility. Stigma has the potential to negatively affect a person's self-esteem, damage relationships, and prevent those suffering from addiction from accessing treatment.

Adolescents, Drug Use and HIV…Oh My!

It is unarguable that the road to "Ending the Epidemic" runs through prevention of HIV transmission in adolescents and young adults of color. Drug use and the behaviors that sometimes accompany it, can increase the risk of contracting HIV. Adolescents who are, "high", intoxicated or inebriated may engage in high risk sexual behavior, such as having impulsive sexual encounters or not using condoms—which significantly increases the risk of exposure to HIV and other sexually transmitted diseases as well. In 2017, about 39,000 new cases of HIV were attributed to sexual contact, and around 2,300 people contracted HIV from injecting drugs.[9]

Children and adolescents are exposed to tobacco, e-cigarettes, alcohol, and other drugs at increasingly younger ages. Social media is loaded with images that promote smoking and drinking as being "cool," fun, and a natural part of being an adolescent. That's why pediatric and adolescent clinicians need to talk to their patients about the perils of drugs and help them understand fact from fiction. The time to begin these conversations is NOW! Children as young as 3 – 5 years old should begin to understand the connection between drug use and consequences – drug use and inability to make good decisions. As your patient gets older, it's okay to let them know how you feel about tobacco use, underage drinking and how social media distorts the dangers of substance misuse. Overcoming our fear and discomfort in talking to young children, adolescents and young adults about substance use and misuse is germane and in part linked to "Ending the Epidemic." **HIV**

REFERENCES

1. Substance Abuse and Mental Health Services Administration (SAMHSA) Results from the 2016 National Survey on Drug Use and Health.
2. Carl E Pickhardt Ph.D. Adolescent Substance Use and The Problem of Denial. Psychology Today. December 11, 2017
3. Williams DG, Patel A, Howard RF. Pharmacogenetics of codeine metabolism in an urban population of children and its implications for analgesic reliability. Br J Anaesth. 2002;89:839–45. [PubMed] [Google Scholar]
4. Drug Facts: High School and Youth Trends from the National Institute on Drug Abuse
5. American Society of Addiction Medicine. Adopted definition, September 15, 2019
6. Ashwood Recovery Student Drug use Survey. January 8, 2018
7. Health & Pharmaceuticals› State of Health› Annual prevalence of Adderall use within grades 8, 10 and 12 in the U.S. 2009-2018
8. Shane, P.; Diamond, G.S.; Mensinger, J.L.; Shera, D.; and Wintersteen, M.B. Impact of victimization on substance abuse treatment outcomes for adolescents in outpatient and residential substance abuse treatment. *The American Journal on Addictions* 15, Issue Supplement s1:s34–s42, 2010.
9. Centers for Disease Control and Prevention. (2018). *HIV surveillance report*.

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Development of an Integrated Drug Utilization Review and Medication Therapy Management Program for Primary HIV Care in the District of Columbia AIDS Drug Assistance Program

THE AIDS DRUG ASSISTANCE PROGRAM (ADAP), established by the United States Congress in 1990 and funded through the Ryan White Comprehensive AIDS Resources Emergency Act, provides HIV positive adults with critical access to a growing number of antiretroviral (ARV) drugs, anti-infective drugs for opportunistic infections, and other HIV-related drugs in all 50 states and U.S. jurisdictions.[1,2] Client engagement and ARV adherence is required to optimize therapy with HIV RNA viral suppression, treatment of significant comorbidities and avoid serious adverse drug reactions.[3] Drug utilization review (DUR) programs are required within state ADAPs and by design, overcome some care limitations. Medication therapy management (MTM) is a newer model of quality improvement that has been integrated into Medicare Part D programs, but not required by state ADAPs.[4] This report describes the integration and initial assessment of an established DUR program and a new MTM program within the District of Columbia ADAP (DC ADAP).

Background

The DC ADAP provides medication and health insurance assistance to eligible District residents. The D.C. Department of Health (DC Health) is awarded grant funding for its Ryan White Part B program; funds are allocated specifically for drug assistance. DC ADAP contracts with a network of pharmacies to dispense formulary drugs for eligible clients. DC ADAP has ~986 beneficiaries, and an average of 1,997 claims monthly, with 23,970 claims reconciled annually. The patient demographics are 66 percent Black or African American, 33 percent White, 0.5 percent Asian, 0.2 percent American Indian or Alaskan Native; 22 percent Hispanic/Latino and 78 percent non-Hispanic; and 71 percent men, 26 percent women, and 3 percent transgender women. DC ADAP has maintained a viral suppression rate of 80 percent since 2015 with a goal to increase to 90 percent by 2020.

A lack of timely integration and coordination of HIV care including underutilization of pharmacists in HIV medication therapy management have been recognized as barriers to optimal care. Strategies are needed to improve the use of pharmacists in HIV care to increase the capacity of HIV service integration with primary medical providers. In 2011, the HIV Medicine Association of the Infectious Disease Society of America (IDSA) and the Ryan White Medical Providers Coalition published a policy statement that included medication management as a critical component of primary HIV care. The policy noted that ideally a clinical pharmacist with HIV expertise should be involved to identify drug interactions, support patient adherence and medication management as well as oversee medication profiles for patients who see multiple providers. The D.C. Health, in collaboration with its infectious disease training and consulting service contractor Clinical Pharmacy Associates, Inc. (CPA), recently began a pilot project to establish an integrated DUR-MTM program to advance quality improvement and optimal client outcomes in the primary care setting. The integrated program supports the D.C. Health 90/90/90/50 Plan released in December 2016 to end the HIV epidemic in D.C. by 2020. Comprehensive core goals of the 90/90/90/50 plan include: 1) 90 percent of D.C. residents with HIV will know their status; 2) 90 percent of D.C. residents with HIV will be in treatment; 3) 90 percent of D.C. residents with HIV in treatment will achieve HIV RNA viral suppression; and 4) D.C. will evidence an overall 50 percent decrease in new HIV cases.

Methods

The launch of the integrated DUR-MTM program required substantial education and team building among key stakeholders including the 1) DC Health, 2) Pharmacy Benefits

Manager (PBM), 3) community pharmacies, 4) medical and clinic provider community, 5) technology providers, i.e. MTM and PBM sources, and 6) members of the HIV/AIDS Drug Advisory Committee (HADAC). CPA led the design, integration, delivery and assessment of the pilot. The pilot period was projected to be six months, but it was extended due to technical challenges with the integration of the member (client), provider (physician and pharmacy) and prescription claims files. The DUR activity consists of monitoring quality of drug use, primarily based on clinical quality indicators from the U.S. Public Health Services (USPHS) Guidelines for Use of Antiretrovirals in Adolescents and Adults. Prospective, concurrent and retrospective DURs are conducted on a routine basis by the point of care pharmacists and by CPA clinical pharmacists. Computerized pharmacy profiles as well as the electronic prescription claim records are utilized to accomplish the reviews. Client records are selected for further concurrent review based on initial evidence of polypharmacy, treatment non-adherence, under or overdosing, significant drug-drug interactions and non-compliance with treatment guidelines. Furthermore, a focused assessment of adherence is conducted on the young adult clients in care. Suboptimal pharmacotherapy and non-adherence issues are often clarified with the pharmacy/physician providers. Clients confirmed to be non-adherent are referred for enrollment in the MTM program.

The MTM process includes an initial call by the CPA clinical pharmacist team whereby each client is informed of the referral to the MTM program and an overview of the procedure, followed by an appointment offer. If an appointment is scheduled, a licensed clinical pharmacist provides the Comprehensive Medication Review (CMR) from the Call Center. Each CMR includes a client health assessment and client updated medication list and medical conditions. Safety alerts identified may include interactions such as drug-drug, drug-allergy, and drug-disease. Potential care gaps identified may include medical conditions lacking therapy and gaps in medication adherence. Safety alerts, potential care gaps as well as additional pharmacist-identified medication-related problems are all addressed as clinically appropriate with a goal of resolution.

The client has an opportunity to ask questions throughout the CMR session, at the end and after the session. Each concern is addressed during or after the CMR session. Client confidentiality is maintained as MTM is within the scope of the clinical pharmacist provider practice. Follow-up calls for clarifications and recommendations are made to clients, the network pharmacy, and/or the physician provider as appropriate. Each client is mailed a Personal Medication List (PML) and a Medication Action Plan (MAP). A Physician summary letter is provided to each client's provider.

Results

The findings for the first 18 months of the integrated DUR-MTM program are available. A summary of the team's quantitative and qualitative work is highlighted in the following sections.

Program Population

The DC ADAP demographics reflect a shift towards an increasing older group of clients with 67.4 percent ≥ 45 years old. This group is increasingly reliant on multiple medications for conditions seen more commonly with older age, i.e., ≥ 65 years or after the onset of chronic conditions including cardiovascular, metabolic and liver disorders. It is in the setting of polypharmacy, comorbidities, changing drug utilization patterns and multiple medical and pharmacy providers that medication management is most challenging and essential. A second notation in the demographics is a higher rate of nonadherence among young adult clients in care. This group represents about 7 percent of the ADAP population but tends to have complex issues with social determinants of health that affect ARV adherence.

TABLE 1: Concurrent and Retrospective DUR Client Group 2

Client	Medications	Concerns/ Resolution
#1	• Abacavir 600 mg/ • Dolutegravir 50 mg /lamivudine 300 mg—1 tablet daily • Atazanavir 300 mg/cobicistat 150 mg- 1 tablet daily	Non-adherence Pharmacy confirms client is non-adherent. **Refer for medication therapy management.**
#2	Abacavir 300 mg/ lamivudine 150 mg/ zidovudine 300 mg—1 tablet twice daily	**Incomplete regimen** **Non-adherence** Per pharmacy, client is currently on Triumeq. Client appears to be consistent with medication refills. Client has alternative insurance.
#3	• Darunavir 800 mg/ cobicistat 150 mg- 1 tablet daily • Dolutegravir 50 mg 1 tablet daily • Etravirine 200 mg 1 tablet twice daily	Drug-interaction COMBO not recommended Cobicistat is a CYP3A4 substrate used to boost darunavir. When used with etravirine, cobicistat levels are decreased. This may lead to loss of efficacy and increased risk of darunavir resistance. Etravirine plus dolutegravir may result in decreased dolutegravir exposure. This interaction is mitigated by adding darunavir/ritonavir or atazanavir/ritonavir to the combination. Cobicistat should be changed to ritonavir in this regimen. **No response from Physician Provider after numerous attempts via telephone and written communication.**

Concurrent and Retrospective DUR- Client Group 1

A total of 768 ADAP client claims data including all age groups from January to May 2017 was screened by the clinical pharmacist team with 23 records selected for further concurrent review of the indicators. Twenty-one (91.3%) client regimens met the criteria for appropriateness based on USPHS guidelines. All clients were receiving appropriate antiretroviral drug dosages. Two clients were receiving regimens deemed to be inappropriate; one client appeared to be receiving only one active ARV (atazanavir/ritonavir). The pharmacy provider confirmed that prescriptions were only presented for atazanavir and ritonavir, but neither was collected, and the claims were reversed. The client was no longer in the DC ADAP. The second client with the inappropriate regimen was receiving the combination of darunavir/cobicistat, etravirine and raltegravir. The use of cobicistat-boosted darunavir with etravirine (a CYP3A inducer) may result in reduced plasma concentrations and pharmacologic effects of cobicistat and subsequently, darunavir.[5] In patients receiving etravirine, atazanavir or darunavir, they should be co-administered with low-dose ritonavir.[5,6] Cobicistat was changed to ritonavir after discussions with the physician provider. Drug-drug interactions were present in seven of the regimens with six requiring monitoring and two requiring dosage or regimen adjustments, which was made for one client. Seven clients, who were confirmed to be non-adherent as evidenced by claims data and verification with pharmacy providers, were referred to the MTM program.

DUR for Young Adults in Care Client Group 1

A clinical pharmacist reviewed claims data for 86 clients (aged 18-30) enrolled in ADAP from January to May of 2017. Fifty clients were receiving ARV or other prescription medications. Seventy-six percent were identified as male, 18 percent as female and 6 percent were designated as "3" with the categorization as "sex unknown". Most clients were receiving integrase strand transfer inhibitor (INSTI)-based regimens (68%) and single tablet regimens (82%). Secondary treatment non-adherence to ARV treatment regimens was verified with pharmacy providers based on pharmacy fill data for 12 of the 50 clients. However, care coverage had expired for four of the clients. The remaining eight clients were referred to the MTM program. Thirty-six (41.9%) clients were non- utilizers of antiretrovirals based on available data.

TABLE 2: Young Adults in Care Client Issues/Concerns and MTM Service Actions/Outcomes Client Group 2

Client #	Regimen	Concerns/issues	Action/Outcome
#1a	• Dolutegravir • Emtricitabine • Tenofovir DF	Last filled in February **1/31/18:** CD4 count 669 cells/mm3 & VL 3,470 copies/mL	**Spanish interpreter** scheduled MTM appointment; client called to cancel and did not respond to repeated attempts to contact. MCM stated that she has made several attempts to contact client without success.
#2a	• Elvitegravir • Cobicistat • Emtricitabine • Tenofovir AF	No refills since January 2018. Client requested refills but needs to be seen by Physician Provider first. **4/26/18:** CD4 count 350 cell/mm^3 & viral load 31,900 copies/mL	**Spanish interpreter** unsuccessful in attempts to contact & schedule appointment. MCM stated that client is hard to reach due to unstable housing and no personal phone.
#3a	• Abacavir • Dolutegravir • Emtricitabine	No fills since December 2017. Scripts transferred to a "specialty" pharmacy. Unclear which specialty pharmacy. **12/18/17:** CD4 count 344 cell/mm3 & viral load 51,233 copies/mL	Phone number on file was client's father; left messages. **Social worker** indicated that client was seen on 6/5/18, is now taking her ARVs and getting better with adherence. 6/20/18: CD4 count 376 cell/mm3 & viral load 9,960 copies/mL
#4a	• Dolutegravir • Emtricitabine • Tenofovir AF	Inconsistent refills. Last filled in May. Filled in November 2017 before that. Recent visit to MD. **5/16/18:** CD4 count 40 cell/mm3 and viral load 510,000 copies/mL	**Spanish interpreter** scheduled appointment for MTM service; client is illiterate in English and Spanish as well as health literacy. During the discussion, client requested to meet in person for service, which was scheduled. Client canceled and stated that he was no longer interested in ARV treatment and was returning to El Salvador. **Care Navigator** and **Physician Provider** confirmed ongoing social and financial issues as well as nonadherence.

Concurrent and Retrospective DUR Client Group 2

DC ADAP claims data from October 2017 to March 2018 was reviewed by the clinical pharmacist team. A total of 690 client records including all age groups were screened for the indicators and 30 were selected for further concurrent review. All the clients were receiving at least two active ARV medications with 73 percent receiving three-drug regimens. Twenty-nine client regimens (96.7%) were considered to be appropriate based on the USPHS Guidelines for Adults and Adolescents. One client was receiving a combination of cobicistat-boosted darunavir, etravirine and dolutegravir. The appropriate PI booster for this regimen is ritonavir.[5, 6] Using the traditional two NRTI backbone-plus one class definition, eight (26.7%) clients received INSTI-based regimens, three (10%) received NNRTI-based regimens, and five (16.6%) were on PI-based regimens. The remaining 14 (46.7%) clients were on a combination of drugs from two or more classes that did not follow the traditional NRTI backbone plus one rule.

Twenty-nine of the 30 clients were receiving appropriate ARV doses. The client who did not meet this criterion was receiving atazanavir 300mg, ritonavir 100mg, efavirenz 600mg, and emtricitabine/tenofovir DF 200mg/300mg, once a day. The atazanavir dose recommended is 400mg when used in combination with efavirenz in ART-naïve patients.[5] Potential drug-drug interactions were present with 14 clients' regimens with one requiring no precautions. Monitoring was required in six of the clients. Seven clients were receiving drug combinations with significant drug interactions that required some dose/regimen adjustment; however, regimen/dosage adjustments had not been made for two of these clients. One client was the previously mentioned case of efavirenz and atazanavir, and the other client was receiving a combination of cobicistat/darunavir, etravirine and dolutegravir, which could result in lower plasma concentrations of cobicistat, darunavir and dolutegravir.[5]

Twelve (40%) clients appeared to be non-adherent based on pharmacy claims data. Many of these were clarified by contacting the pharmacy providers for verification of client's adherence. When pharmacy providers could not provide the necessary information, physician providers were contacted for further clarification. One client was confirmed to be non-adherent and was enrolled in the MTM program. The client with the efavirenz-atazanavir drug interaction was discussed with the physician provider. The physician explained that this client had not been seen at the clinic

TABLE 3: Concurrent and Retrospective DUR Summary—Client Group 2

Category	Number	Percent
Clients contacted	7 of 13	54%
Clients scheduled for CMR of total	6 of 13	46%
Clients scheduled for CMR of those contacted	6 of 8	75%
Clients scheduled who kept their MTM appointment	5 of 6	83%
Clients contacted who declined of those contacted	2 of 8	25%
Clients contacted who need Spanish interpreter	3 of 8	38%
Clients with 2018 viral load <20 copies/mL	3 of 11	27%

TABLE 4: DUR for Young Adults in Care Summary—Client Group 2

Category	Number	Percent
Clients contacted	5 of 8	62.5%
Clients scheduled for CMR of total	2 of 8	25%
Clients scheduled for CMR of those contacted	2 of 5	40%
Clients scheduled who kept their MTM appointment	1 of 2	50%
Clients contacted who declined of those contacted	3 of 5	60%
Clients with contact attempts by Spanish interpreter	7 of 8	88%
Clients with 2018 viral load <20 copies/mL	0 of 8	

for about one year prior to the inquiry. This client was also referred for enrollment in the MTM program. Several attempts via telephone and written communications were made by the clinical pharmacist to reach the physician provider for the cobicistat/darunavir-etravirine-dolutegravir drug interaction without success. Client examples are briefly described below **(see Table 1)**.

DUR for Young Adults in Care Client Group 2

A focused review of only young adults aged 18-30 was conducted during the period of October 2017 and March 2018. A total of 73 young adults were in care. Fifty-five were identified as males, 15 as female and 3 were classified as undetermined or unknown. Fifty-four (~74%) were receiving single tablet regimens. Most (64.4%) clients were on INSTI-based therapies (2 NRTI backbone + INSTI). Sixteen percent were on NNRTI-based regimens and nine were receiving PI-based regimens. The remaining five clients were receiving other drug regimen combinations. Initial screening of adherence as indicated by gaps in prescription refill history generated a list of 27 clients (37%). Further verification with DC ADAP and clarification with pharmacy providers yielded eight non-adherent clients. These clients were referred to the MTM program and have been briefly described in **Table 2.** Intense efforts to connect with non-adherent clients were made by working with ADAP staff and their medical case managers (MCM). In addition, a Spanish interpreter was used to connect with clients who only spoke Spanish and those with limited English proficiency. MTM appointments were made with two of the eight clients (25%). One client kept the first phone appointment; service was not able to be provided because of illiteracy and client requested an in-person appointment which was not kept. None of the non-adherent young adult clients had documented 2018 viral suppression.

MTM

Results from DUR review period October 2017 to March 2018 revealed twenty-one clients who are non-adherent to ARV therapy and referred to the MTM Program. Thirteen clients were from the Concurrent and Retrospective DUR and eight clients were from the targeted DUR for Young Adults in Care. Six of the thirteen clients from the Concurrent DUR were scheduled for a CMR. Five clients kept their appointment and received the service. Three of the five clients received the service via a Spanish interpreter. Two clients refused the service. Three of the five clients who did not receive service had 2018 documentation of virally suppression.

For the DUR for Young Adults in Care, seven clients were provided Spanish interpretation to schedule the MTM appointment. Two of the seven clients were scheduled for a CMR. The one client who kept his appointment was illiterate (reading and writing) in English and Spanish as well as being deficient in health literacy. He requested and scheduled an in-person meeting for service but cancelled the appointment and did not want to reschedule. His most recent viral load was 501,000 copies/mL and his CD4 count was 40 cells/mm^3. Contact was made with his physician provider and care navigator; both confirmed social and financial issues that contributed to non-adherence. The second client cancelled his CMR appointment and did not respond to phone calls thereafter. The remaining six clients were unable to be scheduled for appointments. One client was in a rehabilitation facility in Florida. In addition, four of the eight clients who had 2018 laboratory data available were not virally suppressed.

The following descriptions highlight the MTM actions for the 21 cases referred to the MTM program from the Concurrent and Retrospective DUR Summary Client Group 2 **(see Table 3)** and the DUR for Young Adult Clients Client Group 2 **(see Table 4)**.

The two case descriptions below are examples from the integrated DUR- MTM program.

CASE #1

CN is a 45-year old male with a history of an allergy to Bactrim and Zithromax (ICU admit).

Conditions: HIV, hypertension, diabetes

Medications: abacavir/dolutegravir/lamivudine daily, atazanavir/cobicistat daily, amlodipine 10mg daily and metformin 500mg bid.

CN was referred to the MTM Program because of inconsistent refills of ARV prescriptions. He stated that his primary health insurance does not cover ARVs. He was getting his ARVs at one network pharmacy; his ARVs prescriptions were transferred to another network pharmacy without notification. Through a series of events he said that he did not take his ARVs for two months but is now adherent with a non-detectable viral load. He stated that he has gastrointestinal adverse effects from abacavir/dolutegravir/lamivudine that requires him to consume a large meal before taking it; he also said that he alternates dose timing of his ARVs. His doctor visits are currently every three months. He stated that his diabetes is not well-controlled (recent blood glucose ~190), but recent improvement in A1c from ~9 to 7.6. The CD4 count and viral load on file at DC ADAP dated 3/15/18 were 1189 cells/mm^3 and <20 copies/mL, respectively.

CMR revealed the following concerns:

Safety Alert: Non-adherence

Non-adherence to ARVs increases the risk of viral replication, resistance and HIV transmission. Client was made aware that each ARV product should be taken at the same time every day and to discuss the option of a possible alternative to abacavir/dolutegravir/lamivudine with his doctor.

Care Gap: Omission

Client has diabetes and should be considered for low dose aspirin to reduce the risk of cardiovascular events.

CASE #2

NM is a 35-year old transgender female with a history of allergy to trimethoprim/sulfamethoxazole.

Conditions: HIV, hepatitis C, asthma

Medications: atazanavir 300mg daily, ritonavir 100mg daily, emtricitabine/tenofovir DF daily, conjugated estrogens 1.25mg bid, spironolactone 25mg bid, atovaquone 10mL daily and an unknown inhaler for asthma prn

NM was referred to the MTM Program because of inconsistent refills of ARV prescriptions. Service was provided via a Spanish interpreter. The client admitted to non-adherence and attributed it to social drinking on the weekends. However, this would not account for two-month lapse in ARV refills. She indicated that she was taking one tablespoonful (15mL) of atovaquone daily, was unsure of the name and dose of second drug for transgender therapy as well as the inhaler used for asthma. Validation with the pharmacy provider confirmed the prescribed dose of atovaquone as 10mL daily, transgender hormone therapy as conjugated estrogens 1.25mg bid and Spironolactone 25mg bid. There was no record of a prescription filled for an inhaler. Client stated that she had not been treated for hepatitis C because of drug costs. Discussion with MCM and previous communication with physician provider confirm long history of non-adherence to ARV regimen and making and keeping appointments. The CD4 count and viral load on file at DC ADAP dated 2/23/18 were 264 cells/mm^3 and <29 copies/mL, respectively.

CMR revealed the following concerns:

Safety Alert: Non-adherence

Non-adherence to ARVs increases the risk of viral replication, resistance and HIV transmission. Client admitted to non-adherence; discussion with encouragement and need for adherence was presented.

Care Gap: Omission

Client has not been treated for hepatitis C. Based on discussion with MCM and previous communication with Physician provider, non-adherence is most likely the reason.

Health Literacy

Client lacks knowledge of medication names and doses as well as critical need for ARV adherence.

Discussion/ Conclusion

DUR programs, as required in state ADAPs, help organizations understand the medication use process, discover issues or concerns, interpret, and improve the prescribing, dispensing, administration practices and use of medications.[4] Results are used to guide improvements to the medication use process that can impact the lives of patients. Pharmacists must collaborate with other members of the healthcare team to conduct a successful DUR.[2,3,4] Some of the issues commonly addressed by DURs include drug-disease contraindications, drug-allergy interactions, drug-drug interactions, under-/over-dosing, duplicate therapies, polypharmacy, inappropriate duration of therapy, inappropriate prescribing practices, non-adherence, cost-effectiveness and adverse drug events. Reports of the

findings are generally shared with the interdisciplinary team and oversight committees.

Beyond DUR, is the well-established practice innovation, MTM services, that have been integrated into the DC ADAP program. Several consensus definitions of MTM exist including the following: "A distinct service or group of services that optimize therapeutic outcomes for individual patients." Most notable is that MTM was adopted by CMS for provision of pharmacy benefits for patients when Medicare Part D programs were initially established in 2010 in the US.

Several of the major limitations of the current DUR activities within DC ADAP have been fulfilled with MTM including:

1. Provisions for the time commitment and expertise of the clinical pharmacist team in direct patient care for medication management
2. Access and review of complete medication history within the patient's medical history
3. Greater integration of the client's interdisciplinary team within the community and across the client's continuum of care

There is limited published data on MTM in HIV populations in general and in ADAP populations specifically. Reportedly, at least one ADAP provider has described an MTM program utilizing the call center model in Oregon. The findings from our pilot with DC ADAP demonstrates the feasibility and need for MTM to be integrated into established DUR programs to:

1. Identify and provide client-level medication therapy management by clinical pharmacists to high risk and nonadherent populations
2. Support care integration with the primary care team, including the dispensing pharmacist and the ADAP program
3. Promote quality improvement models
4. Incorporate modern technologies and enhance use of electronic prescription claims and other national prescription utilization databases from dispensing and e- prescribing records

HIV

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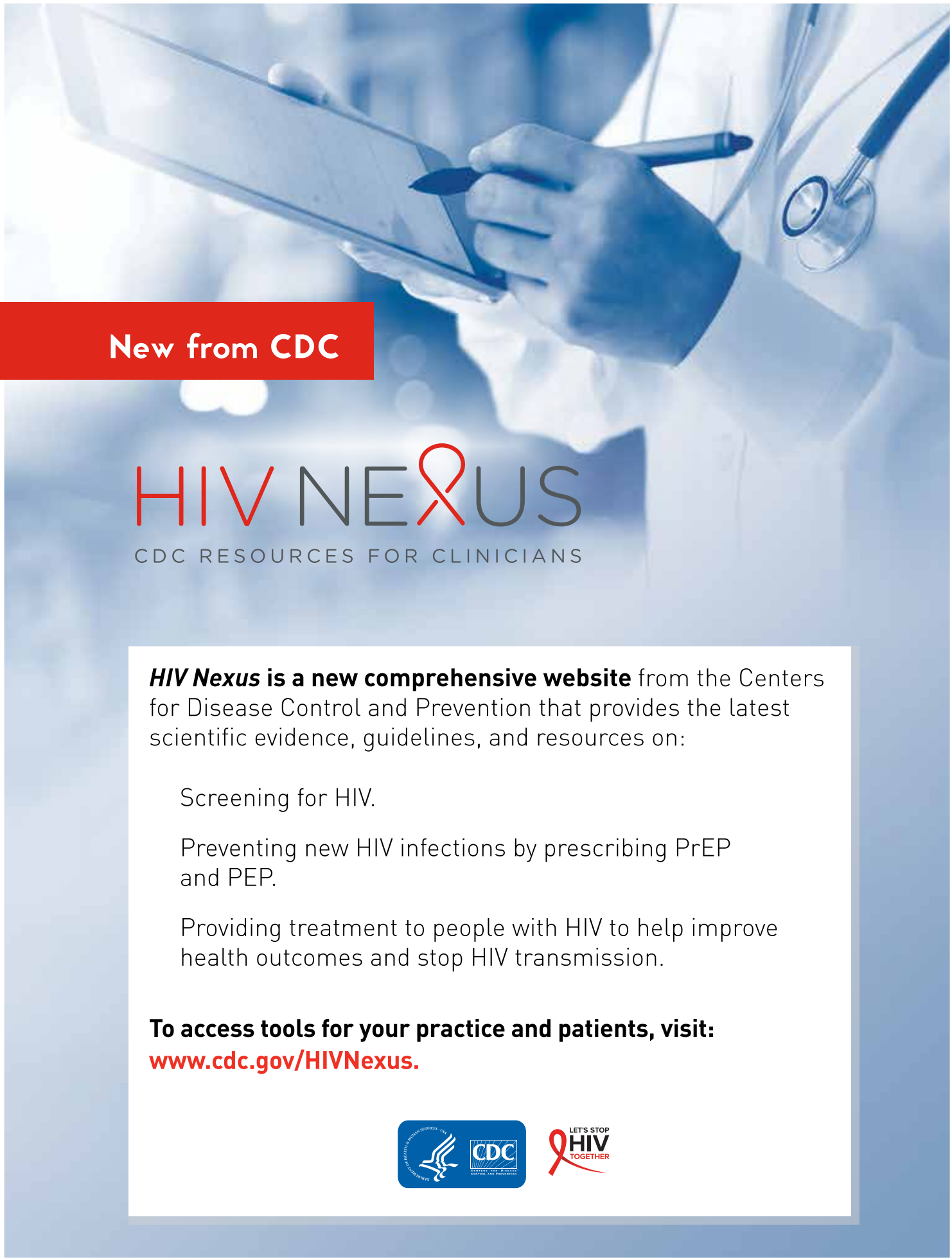
REFERENCES

1. https://hab.hrsa.gov/sites/default/files/hab/About/RyanWhite/habpartbmanual2013.pdf Ryan White Part B Manual
2. https://fas.org/sgp/crs/misc/RL33279.pdf CRS Report for Congress
3. Gallant Jr. et al. Essential Components of effective HIV care: a policy paper of the HIV Medicine Association of the Infectious Diseases Society of America and the Ryan White Medical Providers Coalition. Clin Inf Dis 2011; 53(11) 1043-50.
4. Holtzer C, Ndzerem E, Higgs C et al. Effects of medication adherence in HIV-infected patients by a part D style Medication Therapy Management (MTM) program. 52nd Interscience Conference on Antimicrobials and Chemotherapy (ICAAC). September 9-12, 2012. San Francisco. Abstract H-212.
5. Patterson DL, Swindells S et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med 2000; 133:21-30.
6. Mannheimer S Friedland et al. The consistency of adherence to antiretroviral therapy predicts biologic outcomes for human immunodeficiency virus-infected persons in clinical trials. Clin Infect Dis 2002; 34:1115-21.
7. Bangberg DR, Hecht FM et al. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. Aids 2000; 14:357-66.
8. Harrigan PR, Hogg RS et al. Predictors of HIV drug-resistance mutations in a large antiretroviral-naïve cohort initiating triple antiretroviral therapy. J Infect Dis 2005; 191:339-47.
9. Armstrong EP, Terry AK. Impact of drug use evaluation upon ambulatory pharmacy practice. The Annals of Pharmacotherapy, 1992 December;26: 1546-1553
10. Pulver LK, Tett SE. Drug Utilization review across jurisdictions – a reality or still a distant dream? European Journal of Clinical Pharmacology 2006; 62:97-106
11. Davis S, Rungruangphol PD, Gibson C. Maximizing benefits with the medication use evaluation process. Hospital Pharmacy 2018, Vol. 53 (5):284-285
12. Fanikos J, Jenkins KL, Piazza G, et al. Medication Use Evaluation: Pharmacist rubric for performance improvement. Pharmacotherapy 2014;34(12 Pt 2):5S-13S
13. US Department of Health and Human Services- Aids Info 2018, Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Viewed 6 December 2018, <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0>.
14. Wolters Kluwer, Facts and Comparisons 2018. Interaction Monograph: Cobicistat oral and Etravirine Oral. Viewed 6 December 2018, <http://fco.factsandcomparisons.com/lco/action/msinteract>



New from CDC

HIV NEXUS

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CDC

LET'S STOP HIV TOGETHER

UPDATE

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FEATURED LITERATURE:

Update to the Varicella-Zoster Virus (VZV) Disease Section of the DHHS Adult and Adolescent Opportunistic Infections Guidelines.
Published online September 6, 2019. https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0?utm_source=AIDSinfo&utm_medium=email&utm_campaign=9-5-19-Adult_OI_Guidelines

The DHHS Guidelines for the Prevention and Treatment of Opportunistic Infections recently updated their recommendations on the use of the two FDA-approved vaccines – recombinant zoster vaccine Shingrix® [RZV] and older zoster live vaccine Zostavax® [ZVL] for prevention of herpes zoster in persons with HIV. This information specifically focuses on PLWH age 50 years and older. The guidelines now recommend using RZV instead of ZVL.The newer RZV is a subunit preparation containing recombinant VZV glycoprotein E (gE) and adjuvant AS01B that elicits a much stronger immune response than ZVL. The current schedule for RZV is one IM injection followed by a second "booster" at two to six months. The guidelines note that ZVL may still be used if RZV is not available or cannot be given due to allergy or intolerance. They also note that ZVL is contraindicated in persons with a CD4 count < 200 cells/mm3.

The 2017 approval and recommendations for RZV use were based on several phase 3 randomized, placebo-controlled clinical trials involving >30,000 participants. In these studies, vaccine efficacy against herpes zoster was 97 percent overall and 91 percent in those aged ≥70 years. The most common adverse reactions were pain (78%), myalgia (45%), and fatigue (45%). Grade 3 injection site reactions (pain, redness, and swelling) were reported in 9 percent of vaccine recipients and grade 3 systemic events (myalgia, fatigue, headache, fever, and gastrointestinal symptoms) in 11 percent of recipients. These reactions occurred more frequently after the second dose of RZV. There are some limited data on use of RZV in persons with HIV, and currently ACIP/CDC has not specifically recommended its use in persons with HIV. There are also no data regarding the optimal timing of vaccination for persons who have CD4 counts <200 cells/mm3 or who are not virologically suppressed on ART. It would be reasonable, as with other vaccines to give RZV following initiation of ART with viral suppression and subsequent CD4 count recovery.

COMMENTARY: Following the approval of the RZV in October of 2017 there was such great demand that a subsequent shortage occurred for about one year. The vaccine is again available and we have been recommending for our age-appropriate (>50 years) HIV patients. A few caveats with RZV included: counseling patients about adverse reactions and reassuring them that is it recommended even if they have had shingles in the past. There are insurance reimbursement issues with payers including Medicare, so most of our patients are getting Shingrix® at their community pharmacy or hospital outpatient pharmacy to cover the cost, which is billed under their prescription benefits.

FEATURED LITERATURE:

Kerchberger AM et al. Weight gain associated with Integrase Stand Transfer Inhibitor use in women. Clinical Infectious Diseases,
Published on line: 28 August 2019. https://doi.org/10.1093/cid/ciz853.

Integrase strand-transfer inhibitor (INSTI)-based regimens have become the primary therapies for the majority of persons with HIV disease. Several recent reports have linked these drugs to weight gain – similar to what was seen in the past with protease inhibitors. This paper is from the Women's Interagency HIV Study (WIHS) – a cohort of 10 clinical sites in the U.S. They included 234 women enrolled from 2006 through 2017 who either switched to an INSTI or added an INSTI to their ART regimens. These women were compared to 884 women who were taking non-INSTI ART. Their mean age was approximately 49 years and 61 percent were black. The authors measured weight, body mass index, body fat percentage, along with waist, hip, arm, and thigh circumference. Measurements were obtained at six to 12 months before starting then 6 to eighteen months after starting an INSTI.

Changes in measurements over time in each group were adjusted for race, age, education, smoking status, and baseline ART regimen. Compared to the women maintained on non-integrase regimens, the INSTI group experienced mean greater increases in body weight (2.1kg), BMI (0.8 kg/m^2), and percent body fat (1.4%). They also had 2.0 cm, 1.9 cm, 0.6 cm, and 1.0 cm increases respectively in waist, hip, arm, and thigh circumference. All of these differences were statistically significant and affected nearly 20 percent of the women on an INSTI. No differences in body changes were observed by one specific integrase inhibitor compared to another. The authors note that these increases in adiposity over a short follow-up period indicate an underappreciated health impact of integrase inhibitors, especially in women, and may influence future acceptability of these ART regimens.

COMMENTARY: This study adds to a growing body of data associating INSTI use and weight gain. As the majority of PLWH in the U.S. are now taking an INSTI as part of their ART regimen, greater attention will have to be made to the growing problem of obesity and associated health risks including CVD, diabetes, and hypertension. The gains in both peripheral and central adiposity differ from previously described HIV-associated lipodystrophy. Whether these changes are hormonally-mediated or related to improved appetite and increased caloric intake remains to be determined. I believe it would be reasonable to have this discussion with patients at the start of therapy, however it is not a reason to choose a non-INSTI based regimen.

FEATURED LITERATURE:

Short, W. et al. Use of Recommended Preventive Health Care Services and Variations in HIV Care among Women with HIV in the United States, 2013–2014. Opportunities for Expanded Partnerships in Support of Ending the HIV Epidemic, *JAIDS Nov 1, 2019;82(3):234–244. doi: 10.1097/QAI.0000000000002141*

Along with maintaining patients on effective ART, preventive care and health screening interventions are indicated for the majority of persons living with HIV. Recommendations for preventive health services are issued regularly by various national organizations including the USPSTF, CDC, and other professional societies. There is limited data in regards to how often women who are receiving HIV care are also getting comprehensive medical care. This study used data from the CDC Medical Monitoring Project for the years 2013-2014. The authors used various statistical methods to look at the associations between preventive health screenings, routine HIV care (using CD4 count and viral load measure as proxies), and sociodemographic factors. The study included 2766 women of whom almost half (48%) were 50 years and older. In terms of other demographics, 62 precent were non-Hispanic black, 68 percent were living below the federal poverty level, 67 percent had public health insurance and 37 percent had greater than a high school education. Regarding HIV treatment, 94% were prescribed ART of whom only 66 percent had sustained viral suppression at 12 months. Among women in this cohort who were at least 18 years of age or older, 44 percent were screened for cervical cancer, 28 percent had breast cancer screening, and 35 percent were screened for STIs. Twenty-six percent did not meet six month, and 37 percent did not meet 12-month intervals for obtaining CD4 counts and viral load testing. In multivariable analyses, women with no viral load testing in the past six months were less likely to have viral suppression. The authors note that the delivery of preventive health care in these women was suboptimal and cite the need for interventions to improve uptake and implementation.

COMMENTARY: Overall, these data are rather discouraging but also are five to six years old so I am optimistic that most HIV clinical programs, in particular those that are Ryan White funded are doing better than this cohort of women from the MMP. Newer guidelines have lessened the frequency for mammography and PAP smears which may also improve these data regarding the percent of women screened. However, less frequent visits for CD4 and viral load monitoring – usually every 6 months, make it more challenging to perform all preventive services (including immunizations) at one office visit. Having CQI programs in place that include chart auditing and call-back systems as part of standard office practice are interventions that should help improve these numbers.

FEATURED LITERATURE:

Michos ED et al. Lipid management for the Prevention of Atherosclerotic Heart Disease, *N Engl J Med 2019;381(16):1557-67. DOI: 10.1056/NEJMra1806939*

Because of the growing importance of prevention and treatment of cardiovascular disease in persons with HIV, I have decided to cite an excellent review article on this topic. The content is mainly based on the 2019 ACC-AHA guidelines for cholesterol management for primary prevention of CVD. Here are some key take-home points from the article.

- It has been known since 1961 from Framingham data that an elevated level of low-density lipoprotein (LDL) is a major contributor to atherosclerotic CVD
- Although the general assumption regarding LDL cholesterol is "lower is better," 40 percent of persons with coronary artery disease have normal total cholesterol levels (< 200 mg/dL)
- As a starting point, all adults 40-75 years old should have their overall CVD assessed by using the ACC-AHA risk calculator (cvriskcalculator.com). This should NOT include persons with diabetes or whose LDL is > 190 mg/dL as statin therapy is recommended for these patients
- A low risk ACC-AHA score is less than 5 percent, intermediate risk is 5 to 20 percent, and high-risk is greater than 20 percent
- Statin therapy is recommended for high-risk patients to reduce LDL by 50 percent
- Statin therapy is recommended for intermediate-risk patients to lower LDL by 30 percent
- The presence of risk-enhancing factors, including HIV infection and chronic kidney disease, favor initiation of statin therapy for intermediate risk patients
- For patients at intermediate risk who are statin-intolerant or have concerns about side-effects, coronary artery CT to calculate a calcium score is reasonable. Patients with scores of 0 may defer a statin (except for smokers)

COMMENTARY: The above is a summation of the key points regarding primary prevention of CVD. The article also includes a discussion of secondary prevention and of non-statin therapies including ezetimibe, PCSK9 inhibitors, and N-3 fatty acids. These latter drugs still play a role in persons with elevated triglyceride levels – something that was seen very commonly in the past in patients on boosted-protease inhibitors. Life-style modifications remain very important for primary and secondary prevention of CVD. Shared decision-making regarding risks and benefits of statins is also emphasized in this article.

Readers are also referred to the comprehensive review by Feinstein and Hsue—Characteristics, Prevention, and Management of Cardiovascular Disease in People Living with HIV: A Scientific Statement From the AHA. Circulation. 2019; 140: e98–e124; DOI: 10.1161/CIR.0000000000000695

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