

MANAGEMENT OF HIV- INFECTED ADOLESCENTS

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ADOLESCENTS AND HIV

- Worldwide, there are **1.2 billion** young people
- Among them, **11.8 million** young people are living with HIV/AIDS
- There are approximately **3,000** new HIV infections daily in young people (age **15 – 24** years)
- Teens and young adults one of the most rapidly rising demographic among new infections (**40%** worldwide)

TWO DISTINCT POPULATIONS OF HIV-INFECTED ADOLESCENTS

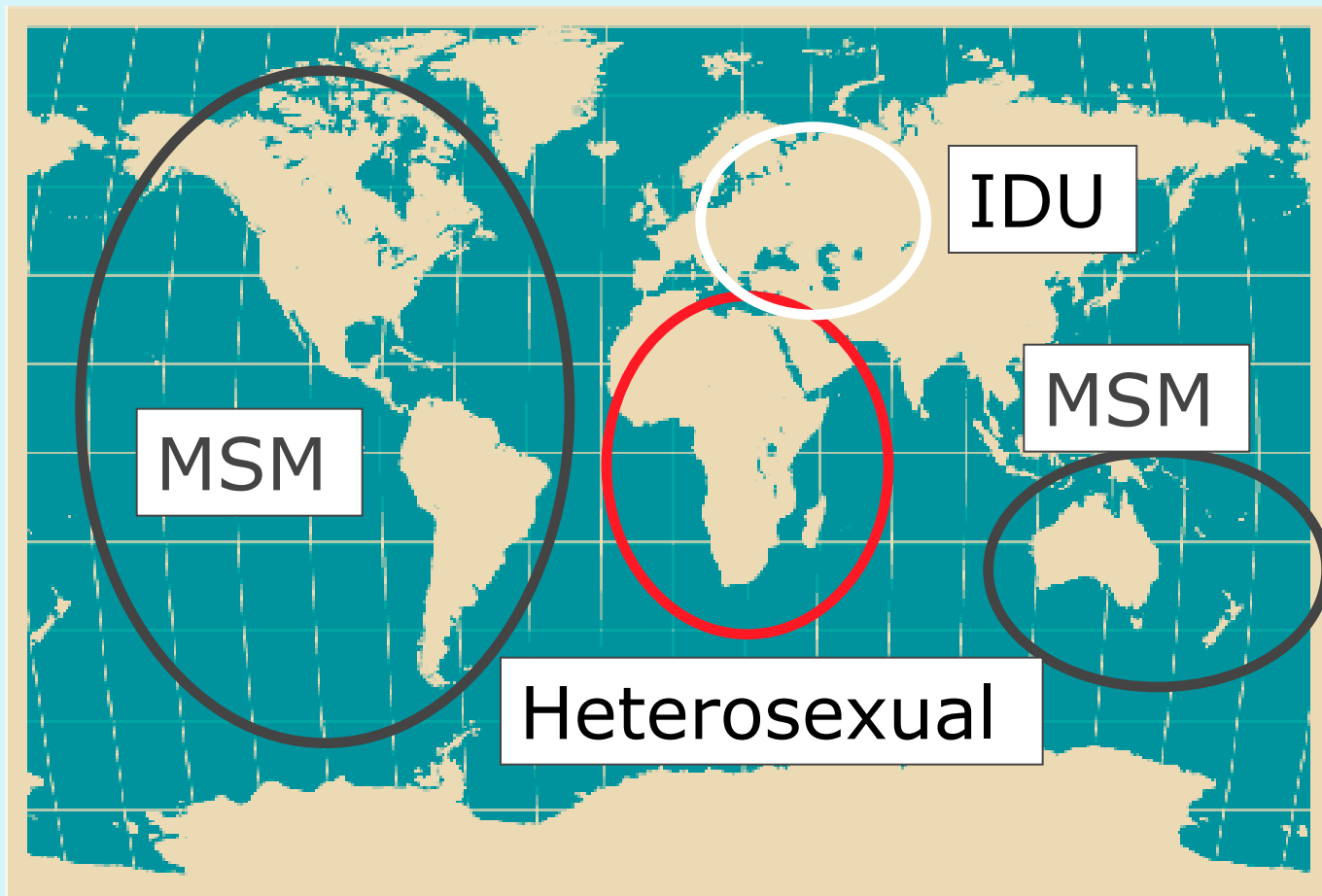


- Disease acquired via perinatal transmission and surviving until adolescence (“Aging-Up”)
- Disease acquired in adolescence via high-risk behaviors



EPIDEMIOLOGY

- Epidemiology varies in different areas of the world



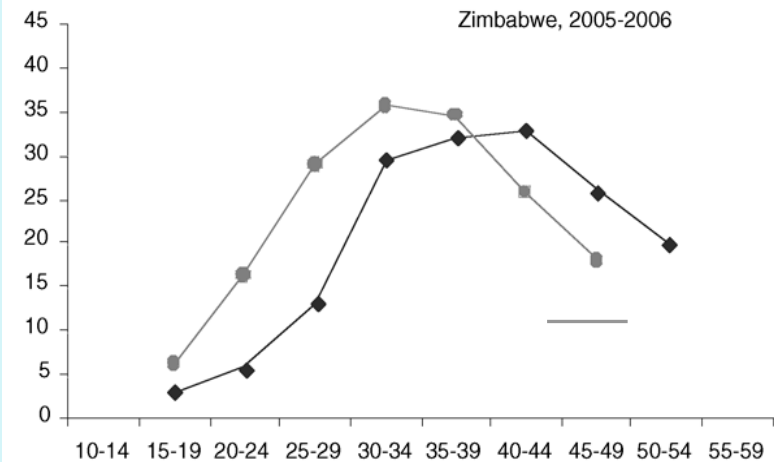
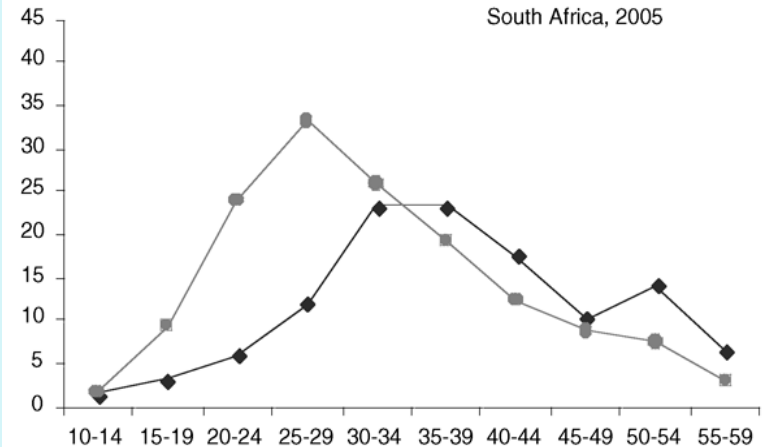
ESTIMATION OF HIV INCIDENCE IN THE US

- MSM represents 56% of new HIV cases
- Black minorities represents 50% of new HIV cases
- Persons, age 13-29 years represents 38% of new HIV cases
- Those 30-39 years represent 30%

ADOLESCENTS IN SOUTHERN AFRICA

- Prevalence increases after 15 years of age
- Increases more rapidly in women than men
- Peaks in women the their 20's and men in their 30's
- Suggest age difference among heterosexual partnerships
- Prevalence higher in urban areas (1.35x)

Age specific seroprevalence rates from data collected from national population based surveys.

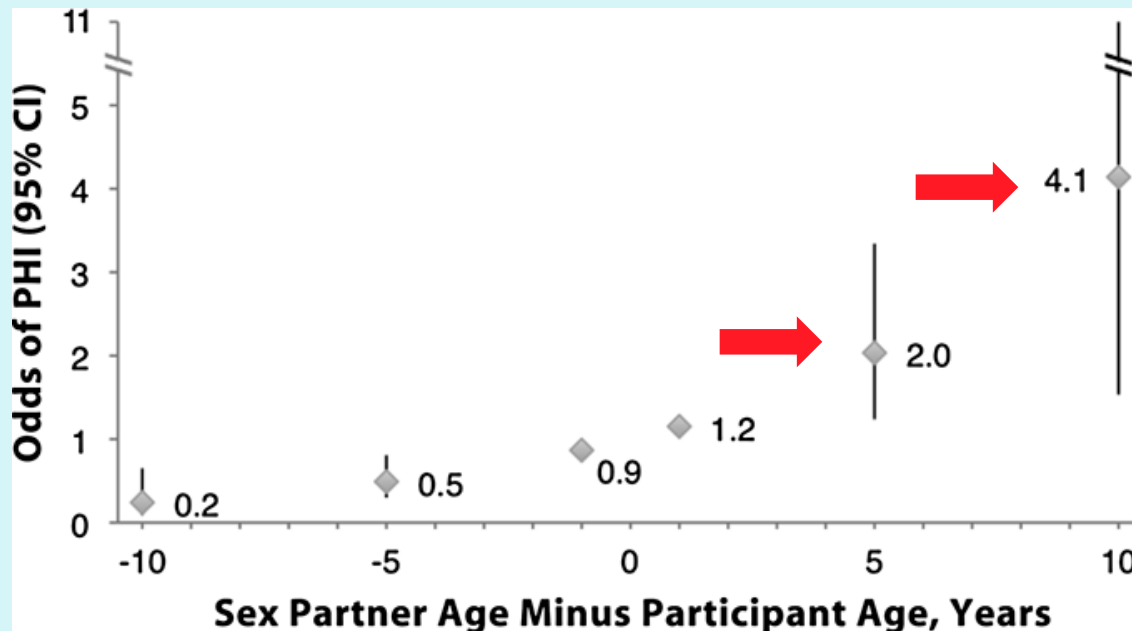


INCREASING INFECTION RATE IN YOUNG MSM - US

- New HIV diagnoses between 2001-2006 in MSM, 13-24 years, increased 12.4% **annually**
- Rate in young black MSM increased more than whites and Hispanics
- Young black MSM was 10-times the overall rate of increase in MSM
- Behavioral studies suggest that young black MSM compared to young white MSM have
 - Fewer sexual partners
 - Less drug use
 - Similar condom usage
 - Increase suspected to be related to higher prevalence among the sexual partners and increase in other STI

RISK FACTORS IN YOUNG MEN WHO HAVE SEX WITH MEN

- Increasing age of sex partner increases risk of recent HIV infection



- An age difference of 5 years 2x the odds of recent HIV infection
- An age difference of 10 years 4x the odds of recent HIV infection

• Adjusted for nonwhite race, sex while intoxicated, and having a serodiscordant or unknown partner

EARLIER SEXUAL DEBUT IN YOUNG MSM A RISK FACTOR FOR HIV INFECTION

- Mean age of MSM debut was 14.5 years (SD 3.2)
- 19% had a MSM sexual debut before the age of 13 years
- Among young MSM with a sexual debut of less than 16 years of age, there was
 - Younger when diagnosed with HIV infection
 - Participated more in exchange sex
 - Used more marijuana
 - Had more emotional/psychological stress
 - More suicide attempts
- No difference in unprotected sex, drug use (other than marijuana), and depressive symptomatology

RISK FACTORS IN YOUNG WOMEN (12-18 YRS, 1995-2000)

HIV-infected young women had more lifetime partners, older partner and had earlier sexual debut compared to HIV-uninfected young women

	HIV + N=153	HIV - N=90	AOR
Number of partners (mean, lifetime)	12.06	7.55	2.23 (1.03-4.82)
Age at 1st vaginal sex (mean)	13.31	14.02	0.74 (0.58-0.95)
Mean difference in age of partners	6.07	4.73	1.06 (1.01-1.12)
Percent reporting a partner was HIV-infected	28%	5.8%	7.46 (3.2-17.4)

HIV/AIDS IN EASTERN EUROPE

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HIV/AIDS in Eastern Europe

NEWS

HIV Moves In on Homeless Youth

Studies have discovered shockingly high HIV prevalence rates in kids who live in the streets of Russia and Ukraine; NGOs are trying to give them new leases on life



ADOLESCENTS IN EASTERN EUROPE

- Estimates suggest that up to 3 million youths are living on the streets in Russia and 150,000 in Ukraine
- Two seroprevalence surveys
 - In 2006, street youth (15- 19 yr) in St. Petersburg, Russia, n=313
 - HIV seroprevalence of 37.4%
 - In 2008, street youth (15-24 yr) in Ukraine (Odesa, Kyiv, and Donetsk), n=929
 - Overall HIV seroprevalence of 18.4%
 - 26.7% in Odesa, 17.1% among 15-17 year olds and 33% among 18-24 year olds

RISK FACTORS IN STREET YOUTH IN RUSSIA AND UKRAINE

- In both St. Petersburg and Ukraine studies, there were high rates of sexually activity (>90%), multiple partners, injection drug use (68.2% vs. 33.7%), prior STIs

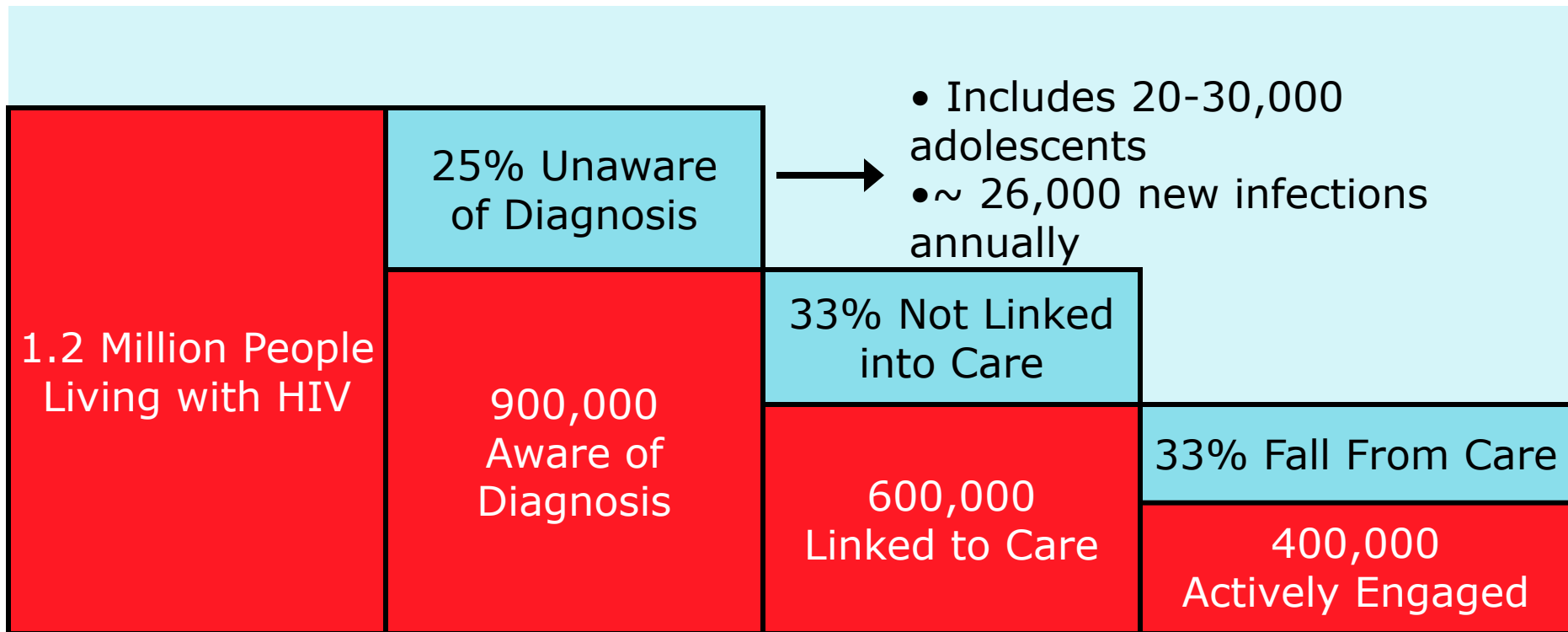
Risk Factor	AOR, Russia	AOR, Ukraine
Orphaned	3.3 (double); 1.8 (single)	1.7
No place to live	2.4	1.9
Injection drug use	23	9
Drug use		5
Needle sharing	13.3	6.8
Diagnosed with STI	2.1	2.8
History of anal sex		1.8
Exchanging sex		4.8
Time on street > 3 yr		2

Kissin, AIDS 21:2333, 2007; Robbins, Int J STD AIDS 21:489, 2010

EPIDEMIOLOGY

- **Epidemiology varies in different areas of the world**
- **In US, Western Europe, and Australia, adolescent epidemic being driven by young men who have sex with men (MSM)**
- **In Southern Africa, heterosexual transmission most likely**
- **Eastern Europe, intravenous drug use**

THE HIV/AIDS EPIDEMIC IN THE USA



ACCESSING AND ENGAGING IN HEALTHCARE SERVICES – BARRIERS

- **11% of youth with HIV in the US receive adequate medical care**
- **Paying for services problematic - low-income people aged 19-20 have the highest uninsured rate - 47.7%**
- **Gap between testing and medical care facilities is great**
- **Confidentiality issues and parental permission for care may also present barriers**

DELAYED ENTRY INTO CARE OF HIV-INFECTED YOUTH, MEMPHIS, TN

- Examined risk factors for delayed entry into care (>60 days from +HIV test awareness) in 202 youth infected via high risk behavior
- 38% had delayed entry into care
- Unstable home (> 3 locations within past year) was the largest risk factor associated with delayed entry – AOR 1.5 (95%CI 1.0-2.1)
- Virologic and immunologic parameters no different between immediate entry into care and delayed entry

FAILURE TO REMAIN IN CARE

- US adolescents (age 17-24 years) are more likely to drop out of care compared to adults (age 25 – 40 years), 43.5% vs. 10.9%
- In Memphis cohort, 29% failed to remain engaged in care
- South African lost to follow up rates differ by mode of infection
 - Perinatally-infected adolescents – 3.9 per 100 patient years
 - All adolescents (age 9-19 years) – 7.2 per 100 patient years
 - Young adults (age 20-28 years) – 10.2 per 100 patient years
- Factors associated with failure to remain in care
 - No health care insurance - AOR 2.8 (95%CI 1.1–6.9)
 - Caring for a child - AOR 1.8 (95%CI 1.0–3.1)
 - High school drop-outs - AOR 4.0 (95%CI 1.1–15)

FACTORS ENCOURAGING ONGOING ENGAGEMENT IN CARE

- Among 224 clients, only 11.5% of follow-up visits missed
- Factors associated with not missing visits
 - Receiving any program services
 - Feeling respected
 - Younger age
 - Ever feeling depressed
- Low CD4 count or being Latino associated with being more likely to miss a visit

TREATMENT OF HIV INFECTION IN ADOLESCENTS

- Follow local current adult/adolescent guidelines. In US,
 - Treat all infected persons but strength of recommendation based on CD4, if less than 350, all favor treatment
 - AIDS-defining illness
 - HIV nephropathy
 - HIV/HBV coinfection
- Patients starting ART should be
 - Willing and able to commit to treatment and
 - should understand the benefits and risks of therapy and
 - the importance of adherence

ANTIRETROVIRAL THERAPY INITIATION IN ADOLESCENTS AND YOUNG ADULTS

- Adolescents and young adults infected via high risk behaviors start therapy later than older adults
 - Age 18-24 years – initiation at a median of 204 days
 - Age 25-29 years, 125 days
 - Age 30-49 years, 153 days
 - > age 50 years, 145 days

ANTIRETROVIRAL THERAPY INITIATION IN ADOLESCENTS AND YOUNG ADULTS

- Successful virologic control is less than in adults
- Poor adherence to ART regimen is the greatest risk for failure to suppress

Cohort	% with Virologic Suppression at 1 Year
PACTG 381 (age 13-21)	52
South African (age 11-19)	46
South African (age 20-30)	56
COHERE (European, age 13-17)	46
COHERE (European, age 18-29)	50
Haiti (age 13-25)	49

Flynn J Infect Dis 190:271, 2004, Rudy AIDS Res Hum Retroviruses 22:213,2006, Flynn AIDS Res Hum Retroviruses 23:1208,2007 ; Nachega et al, JAIDS 51:65, 2009; COHERE AIDS 22:143, 2008; Charles, Bulletin of WHO, December 2008,86

CHARACTERISTICS ASSOCIATED WITH REDUCED ADHERENCE IN ADOLESCENTS

- Patient Characteristics
- Structural Factors
- ART Related Factors
- Social Factors
- Mental Health Factors

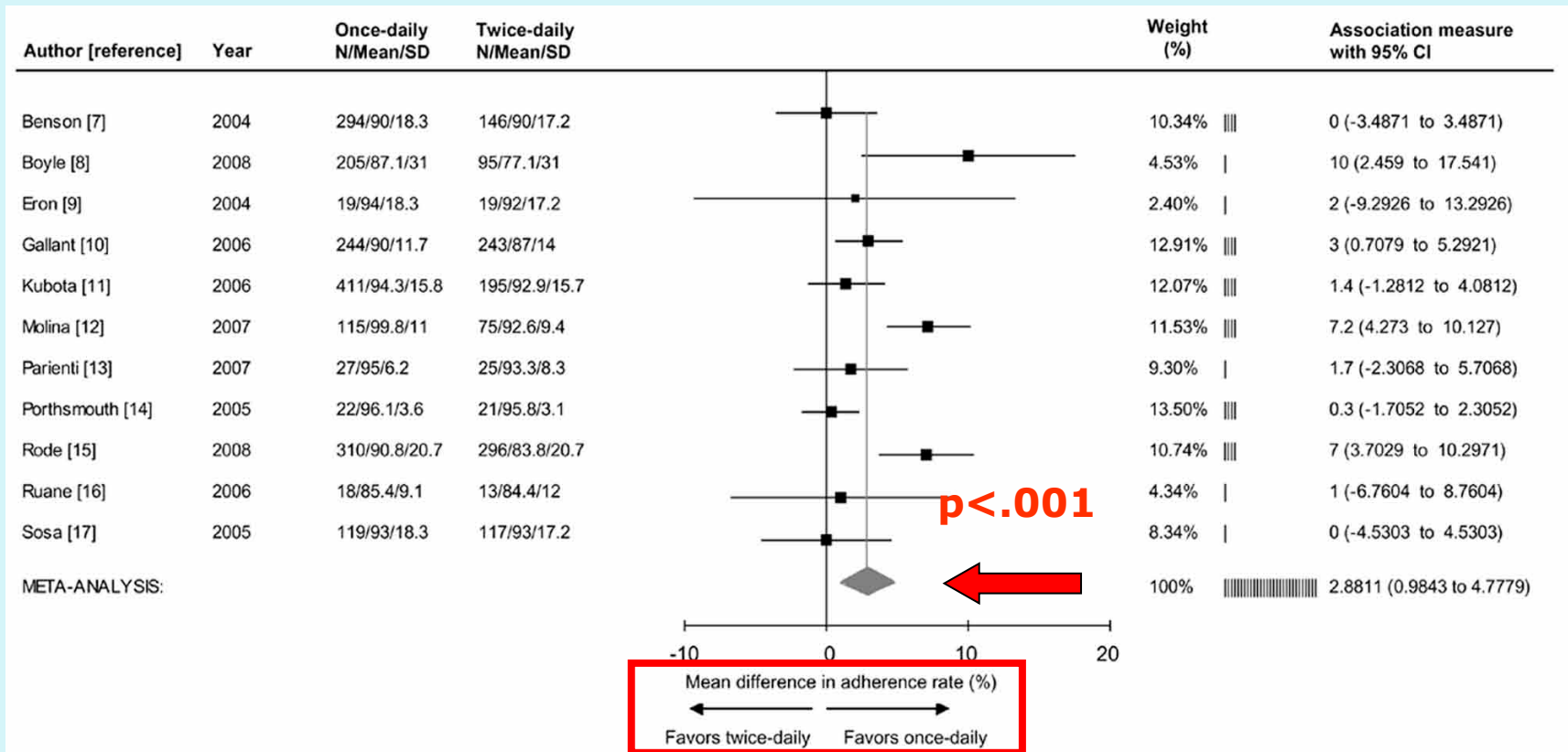
Reisner, Top HIV Med 17:14, 2009; Rudy, AIDS Pt Care STD 23:185, 2009; Murphy, Arch Pediatr Adolesc Med 159:764, 2005; Williams, Pediatrics 118:e745, 2006; Vreeman, Pediatr Infect Dis J 27:686, 2008; Filho, Intern J STD AIDS 19:685, 208; Nachege et al, JAIDS 51:65, 2009; Rudy AIDS Pt Care STD 24:97, 2010

STRATEGIES TO ASSIST WITH ADHERENCE

- Education
- Technologic innovations (phone or beeper reminders, text messaging, social networks)
- Regimen simplification (once daily, de-intensification, STI)
- Directly observed therapy (DOT)
- Few data from randomized clinical trials

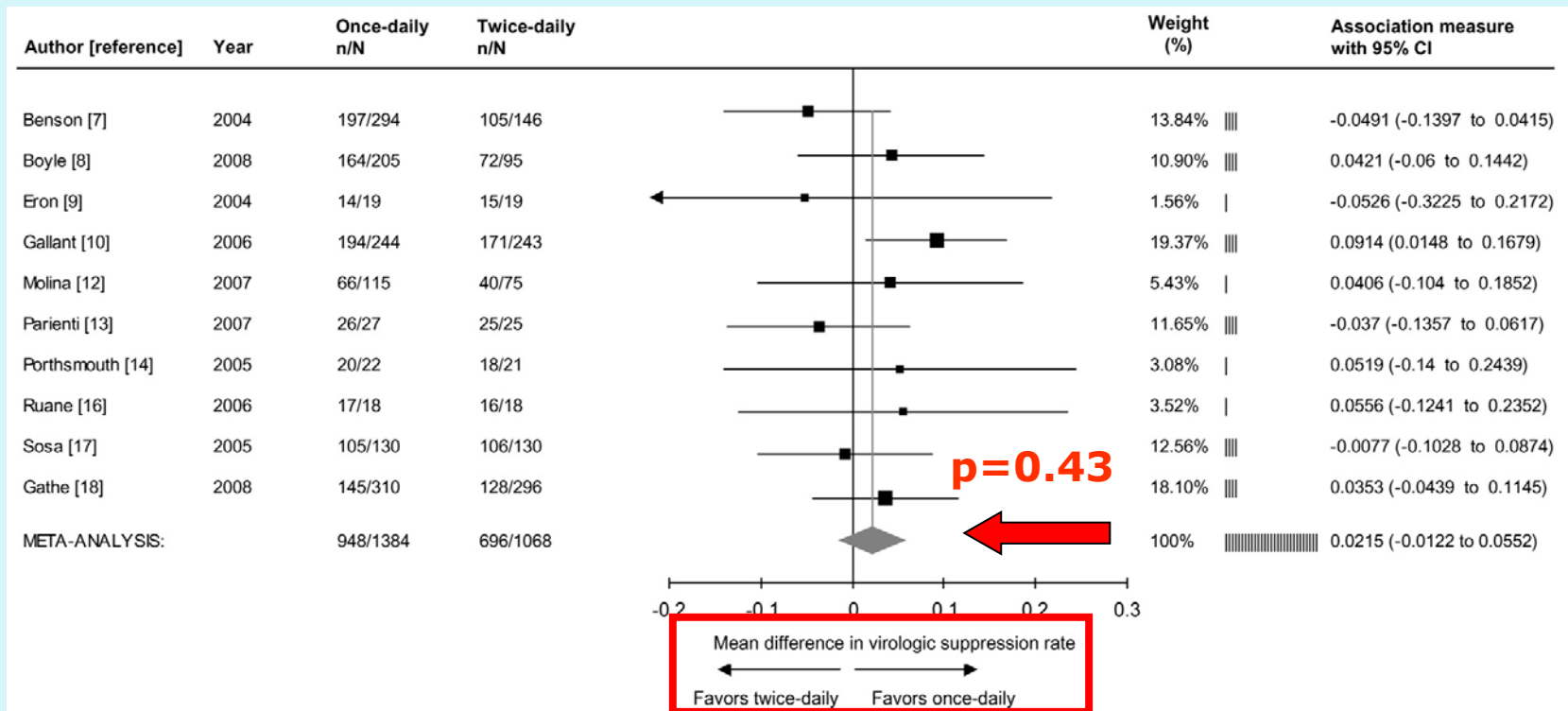
ONCE VS. TWICE DAILY DOSING

- Meta-Analysis of 11 adult RCTs demonstrates improved adherence with QD regimens



ONCE VS. TWICE DAILY DOSING

- But, no difference in virologic suppression rate

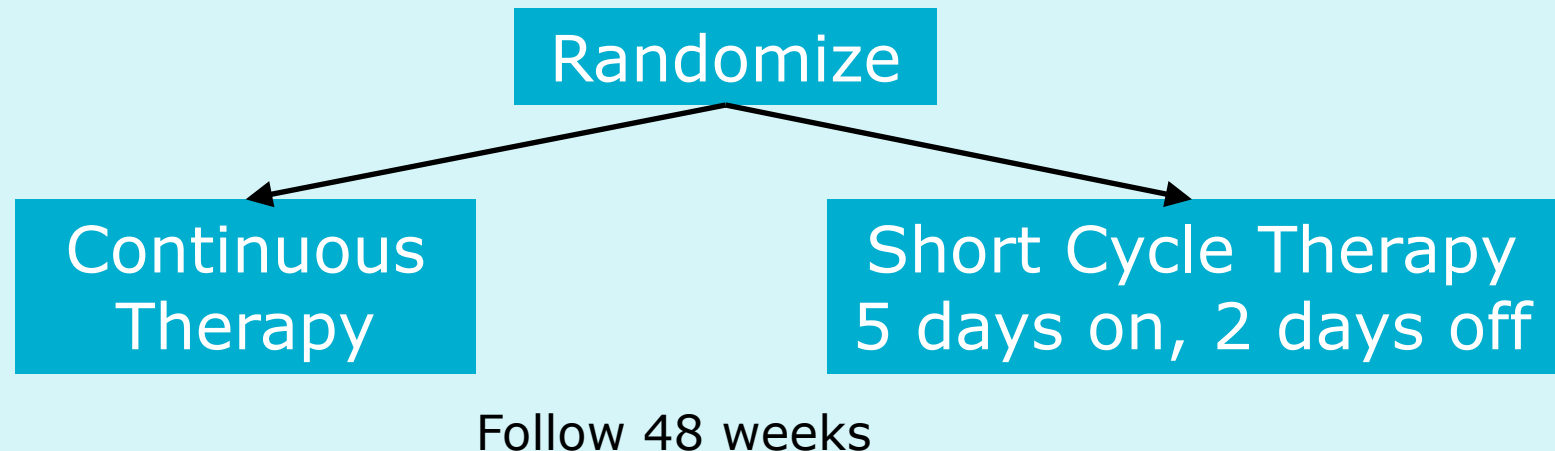


STRUCTURED TREATMENT INTERRUPTIONS – ATN 015

- Adolescents with VL less than 400 for at 6 months and CD4+ count above 350 cells/mL who were receiving Protease Inhibitor therapy
- Randomized to 4 days on then 3 days off
- Stopped STI for viral rebound, 30% drop in CD4+ count or pregnancy
- Rebound associated with prior AIDS diagnosis ($p=0.004$) and perinatal mode of infection ($p=0.02$)

STRUCTURED TREATMENT INTERRUPTION

- Two adult studies show promise for a 5 day on, 2 day off efavirenz based regimen
- Also being studied in children and adolescents in PENTA 16 - BREATHER
 - Age 8 to 21 years
 - Viral load < 50 copies/mL for at least 12 months (a single blip between 50 and 1000 is allowed)
 - First HAART regimen
 - CD4 cell count \geq 350



REGIMEN SIMPLIFICATION

- Simplified maintenance therapy using LPV/r, DRV/r, ATV/r after initial viral suppression
- Benefits of potential reduction of drug related adverse events, costs, and pill burden
- Not currently recommended in adults due to higher rates of low level viremia with simplified regimen
- Ongoing study (ATN 061) in adolescents

MENTAL HEALTH

- Role of HIV infection in mental health disorders is still not clear
- Many risk factors for mental health disorders overlap with those for HIV (e.g., poverty, disrupted home life, history of mental illness or substance abuse)
- Mental health disorders have been associated with increases in sexual risk behavior, substance abuse, and poorer medication adherence

MENTAL HEALTH DISORDERS IN ADOLESCENTS INFECTED VIA HIGH RISK BEHAVIORS

Table 2. Previous and Current Psychiatric Diagnoses

	No. (%) of Subjects (N = 34)
Previous Psychiatric Information	
History of psychiatric referral	24 (71)
History of psychiatric hospitalization	10 (29)
History of psychotropic medication	8 (24)
History of documented psychiatric diagnosis	18 (53)
Previous psychiatric diagnoses	
Conduct disorder	9 (26)
Mood disorder (depression, dysthymia)	9 (26)
Adjustment disorder	10 (29)
Substance abuse	4 (12)
SCID-P Diagnosis*	
No diagnosis	5 (15)
Mood disorder ever	23 (68)
Substance abuse/dependence ever	20 (59)
Current major depression	15 (44)
Concurrently using substances	6 (40)†
Concurrently not using substances	9 (60)†

*Does not include attention-deficit/hyperactivity disorder, conduct disorder, or gender identity disorder. SCID-P indicates Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition.

†Refers only to those with current major depression.

- 34 adolescents, age 16 – 21 years, mood disorders, substance abuse, and depression common
- ADHD, conduct disorders, gender identity disorders not included

MENTAL HEALTH DISORDERS IN ADOLESCENTS INFECTED VIA HIGH RISK BEHAVIORS

TABLE 3. FREQUENCY OF PSYCHOLOGICAL DISORDERS
ASSESSED IN HIV-POSITIVE YOUTH (n = 174)

Variable	Females (n = 58) (%)	Males (n = 116) (%)	Total (%)	χ^2
Major depressive disorder	20	12.9	14.8	1.446, <i>n.s.</i>
Suicidal ideation past 1 month	25.5	20.7	21.6	1.388, <i>n.s.</i>
Anxiety disorder	20	15.5	17	0.532, <i>n.s.</i>
Panic disorder	14.5	6	9.1	3.377, <i>n.s.</i>
Alcohol abuse	7.3	19	15.3	3.957, <i>p</i> < 0.05
Drug abuse	27.3	32.2	31.4	0.421, <i>n.s.</i>
Posttraumatic stress disorder	30.9	27.8	28	0.172, <i>n.s.</i>

- High rates of posttraumatic stress disorder, mood disorders also reported
- Memphis Clinic Experience
 - 15% prior diagnosis of major depression
 - 8% prior suicidal ideation

HISTORY OF PHYSICAL AND SEXUAL ABUSE

	Chicago	Memphis
Physical		17%
Adult	16.7%	
Child	24.3%	
Sexual		41%
Adult	14.5%	
Child	27.8%	
Witness Family Violence	44.4%	

- Exposure to personal violence high
- Hypothesized to impact sexual risk taking behaviors

ADOLESCENTS, HIV, AND PREGNANCY

- In US, of 242 US adolescents, 61 pregnancies reported over 3 year, (25%, 20.6/100 person years); No reported outcome for infants
- In London, 67 pregnancies in 58 adolescents, age 13-19
 - 82% unplanned
 - One infant infected (1.5%)

CONCLUSIONS

- Highest incidence of HIV infection is in adolescents and young adults
- Route of infection variable and related to location
- Risk factors are predictable – risky sexual activity, IDU
- Linking and engaging in care may be difficult
- Treatment with antiretroviral therapy is initiated later and is associated with lower rates of viral suppression compared to adults
- Adherence is the most common risk for treatment failure
- Once daily and simplified regimens show promise
- Co-morbid mental health conditions complicate management



Thanks for
Your Attention!