HIV, ART and Adolescence - The Perfect Storm

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The Path to Adulthood

- Epidemiologic snapshot
- Biomedical health outcomes
- Psychosocial & behavioral outcomes
- Sexual & reproductive health
- Transition from pediatric to adult care

Objectives

- To review the global estimates for adolescents, 10-19 years of age, living with HIV infection
- To describe biomedical conditions and outcomes of adolescents with perinatal HIV infection
- To describe psychosocial and behavioral outcomes of adolescents with perinatal HIV infection
- To identify the contributions of HIV, antiretroviral treatment (ART) and the developmental stage of adolescence to health outcomes among adolescents with perinatal HIV infection

GLOBAL OVERVIEW

Global summary of the AIDS epidemic | 2013

Number of people living with HIV	Total	35.0 million [33.2 million – 37.2 million]
	Adults	31.8 million [30.1 million – 33.7 million]
	Women	16.0 million [15.2 million – 16.9 million]
	Children (<15 years)	3.2 million [2.9 million – 3.5 million]
People newly infected with HIV in 2013	Total	2.1 million [1.9 million – 2.4 million]
	Adults	1.9 million [1.7 million – 2.1 million]
	Children (<15 years)	240 000 [210 000 – 280 000]
AIDS deaths in 2013	Total	1.5 million [1.4 million – 1.7 million]
	Adults	1.3 million [1.2 million – 1.5 million]
	Children (<15 years)	190 000 [170 000 – 220 000]

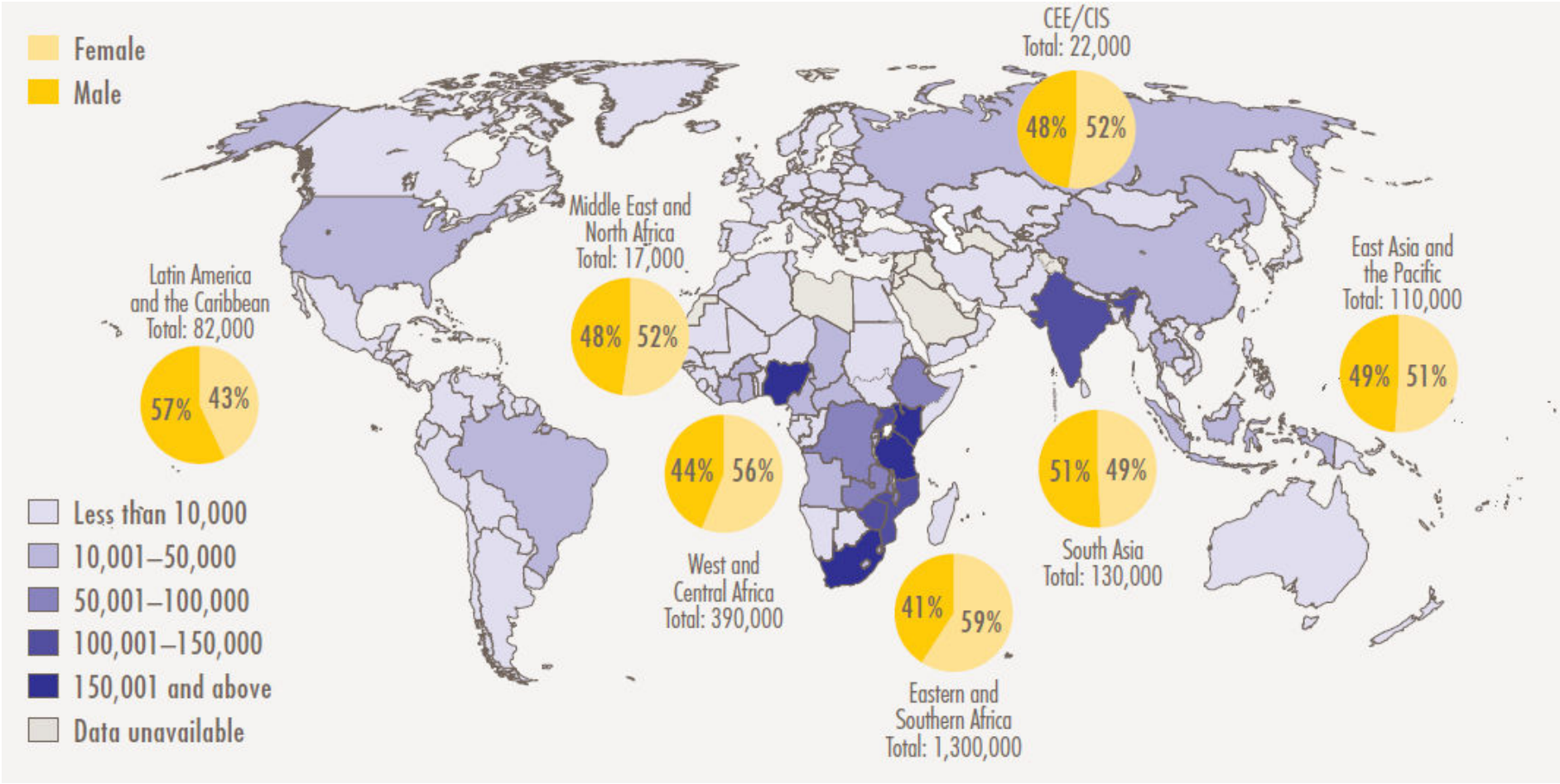
UNAIDS

Epidemiologic snapshot: HIV infection among adolescents

- Globally, it is estimated that there are approximately 2.1 million adolescents (**10-19 years**) living with HIV
  - Overlapping definitions of adolescents (10-19 yrs) and youth (15-24 yrs).
    - 10-15 yrs included with children; 15-19 yrs included with adults
    - Includes **perinata**l and **behavioral** acquisition
  - There were an estimated 250,000 new HIV infections among adolescents (15-19yrs) in 2013
    - 2/3 of all new adolescent infections occurred among girls
  - Approximately 80% live in Sub Saharan Africa
  - Approximately 58% of adolescents with HIV are female

UNICEF, Taking Stock Report, 2013; All In: Global Strategy Report, UNAIDS, 2014

Estimated number of adolescents living with HIV by UNICEF region, 2013



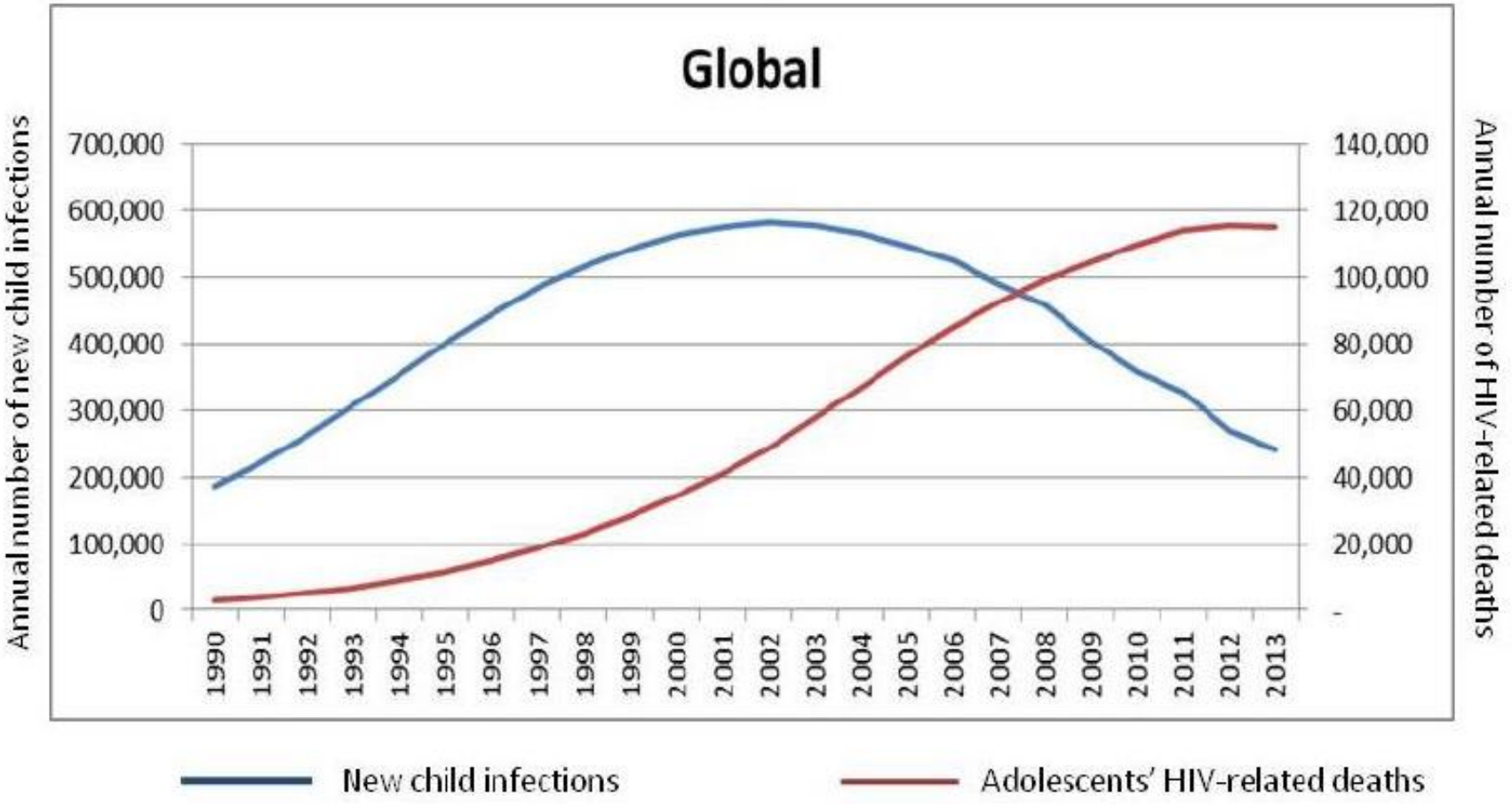
UNICEF, Taking Stock Report, 2013

HIV-related mortality remains high among adolescents

- There were ~120,000 AIDS-related deaths among adolescents in 2013
  - HIV/AIDS 2nd leading cause of death among *adolescents* globally, following road traffic injuries
- From 2005-2013, modeling suggests a 50% increase in HIV-related mortality among *adolescents*
  - Only group in which HIV-related deaths have risen

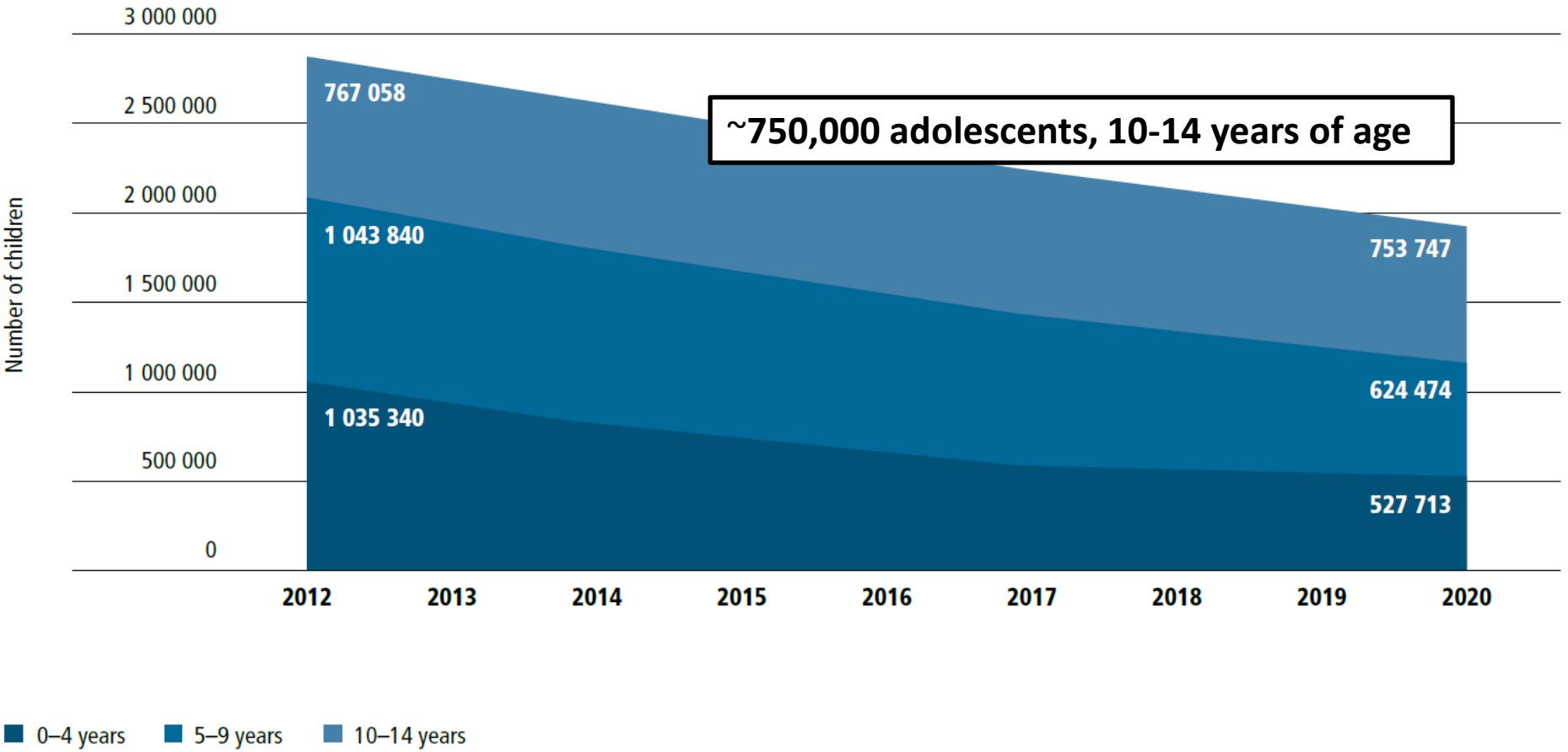
UNICEF, Taking Stock Report, 2013; All In: Global Strategy Report, UNAIDS, 2014

Numbers of HIV-related deaths among adolescents and new child infections



UNICEF, Taking Stock Report, 2013; All In: Global Strategy Report, UNAIDS, 2014

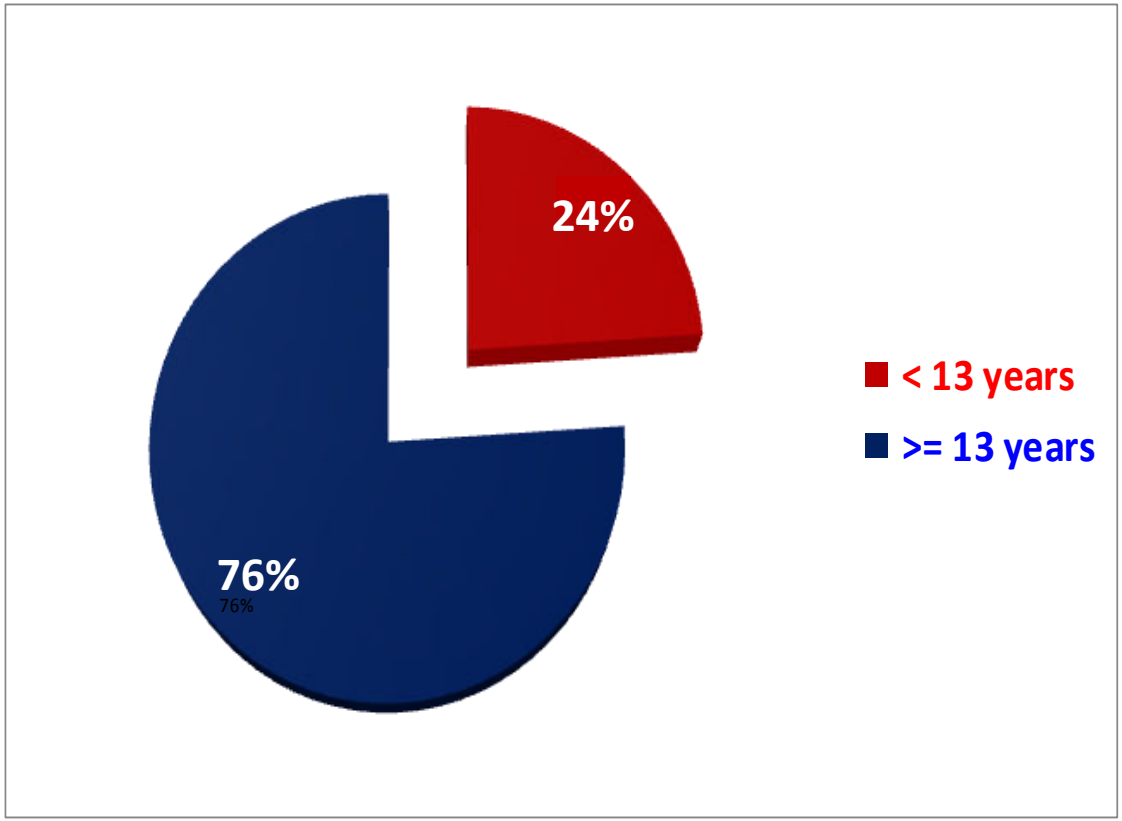
Number of children & adolescents (10-14yrs) with HIV projected in 21 priority countries in Sub Saharan Africa in 2020.



WHO March 2014 Supplement to 2013 Guidelines

A snapshot of perinatal HIV in the US

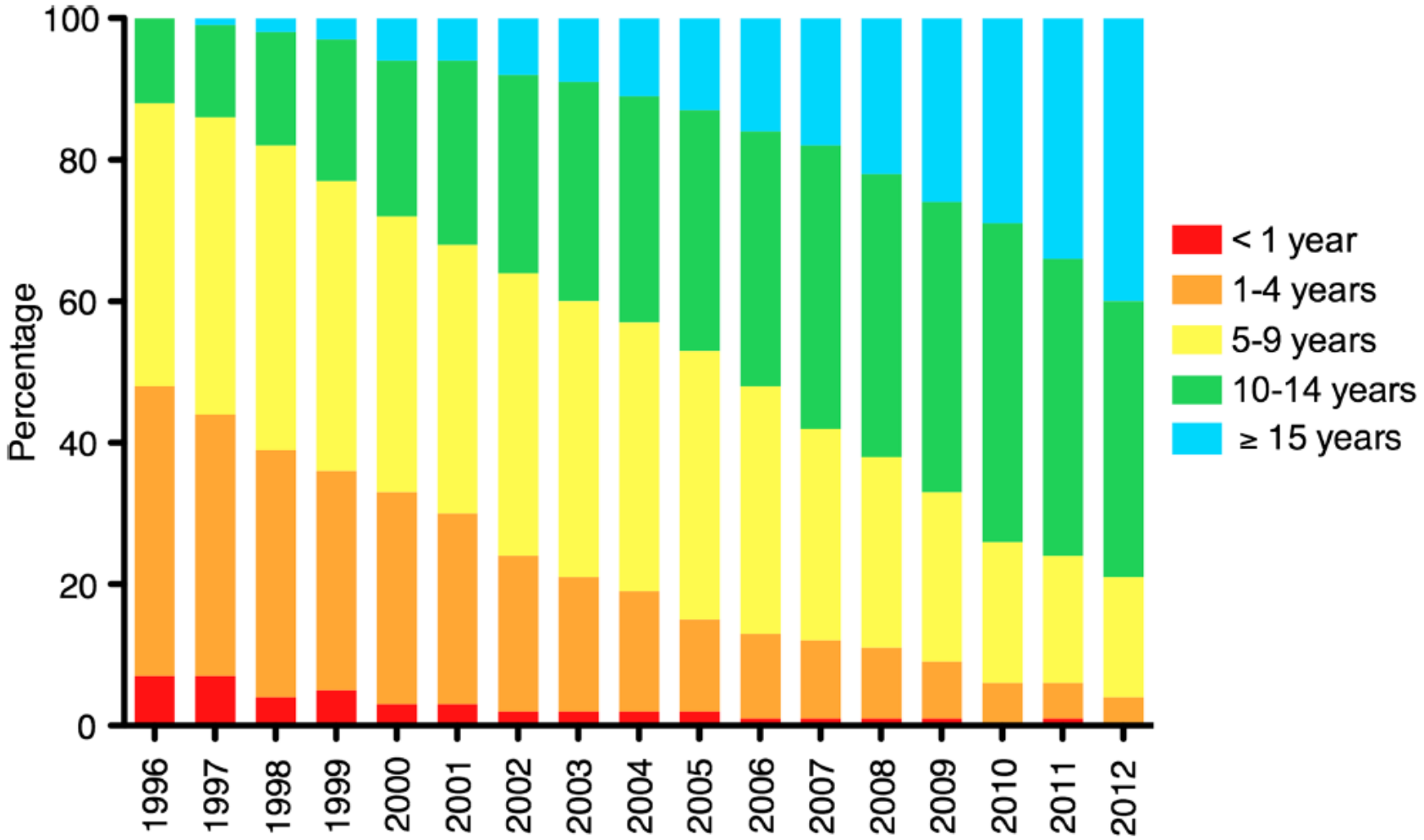
10,798 persons with perinatal HIV living in the US in 2010



NYC: 2,449 children with living with perinatal HIV *(NYCDOH, 2012)*

- 13% < 13 years
- 76% - 13-24 years
- 11% > 24 years

Age distribution of 1131 HIV+ children in CHIPS cohort, UK



Bamford, *Arch Dis Child* 2015

BIOMEDICAL HEALTH OUTCOMES

Demographic profile of adolescents with perinatal HIV infection

- Globally, vulnerable families, often affected by poverty, violence, limited health care and educational resources
- Disruptions in caregiving due to parental illness, death and poverty
- In some countries, parental substance abuse and untreated mental illness have decimated families
- In many countries, youth with perinatal HIV are from ethnic minorities and other disenfranchised populations who have coped with racism and discrimination, and now must cope with *HIV stigma*

Biomedical profile of youth with perinatal HIV infection

- Two overlapping cohorts of perinatally HIV-infected adolescents
  - Aging children identified and treated during infancy and/or childhood
  - Newly identified during adolescence
    - It is estimated untreated infants with perinatal infection have a ~ 20-30% probability of survival to >10 years
    - Asymptomatic or with history of multiple nonspecific health conditions (URI, skin disease, recurrent diarrhea, recurrent infections)

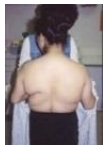
- Among those who survive, globally, youth with perinatal HIV have multiple health problems as a consequences of:
  - Late identification and late ART availability/initiation
  - Suboptimal regimens during early childhood
  - Antiretroviral-associated toxicities

Common conditions among adolescents with untreated perinatal HIV

- **Chronic lung disease**: untreated lymphocytic interstitial pneumonia with bronchiectasis and cor pulmonale; small airways disease with constrictive obliterative bronchiolitis
- **Cardiac disease**: dilated cardiomyopathy, pericardial effusion, LV diastolic dysfunction, increased LV thickness, decreased LV fractional shortening, pulmonary hypertension
- **Growth Failure**: stunting and pubertal delay
- **Opportunistic infections**: crypto, TB, vaccine preventable illnesses
- **Malignancies**: Burkitts lymphoma and Kaposi Sarcoma
- **Skin disease**: nonspecific rashes, papular pruritic eruptions, angular cheilitis, molluscum contagiosum, herpes zoster, warts
- **Othe**r: HIV nephropathy, low bone mineral density

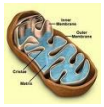
Lowenthal *et al, Lancet 2014*

Complications of HIV and ART for adolescents with perinatal HIV

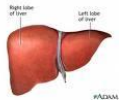


- Metabolic complications

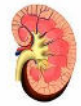
- Bone disease



- Mitochondrial toxicity



- Liver disease



- Renal Disease

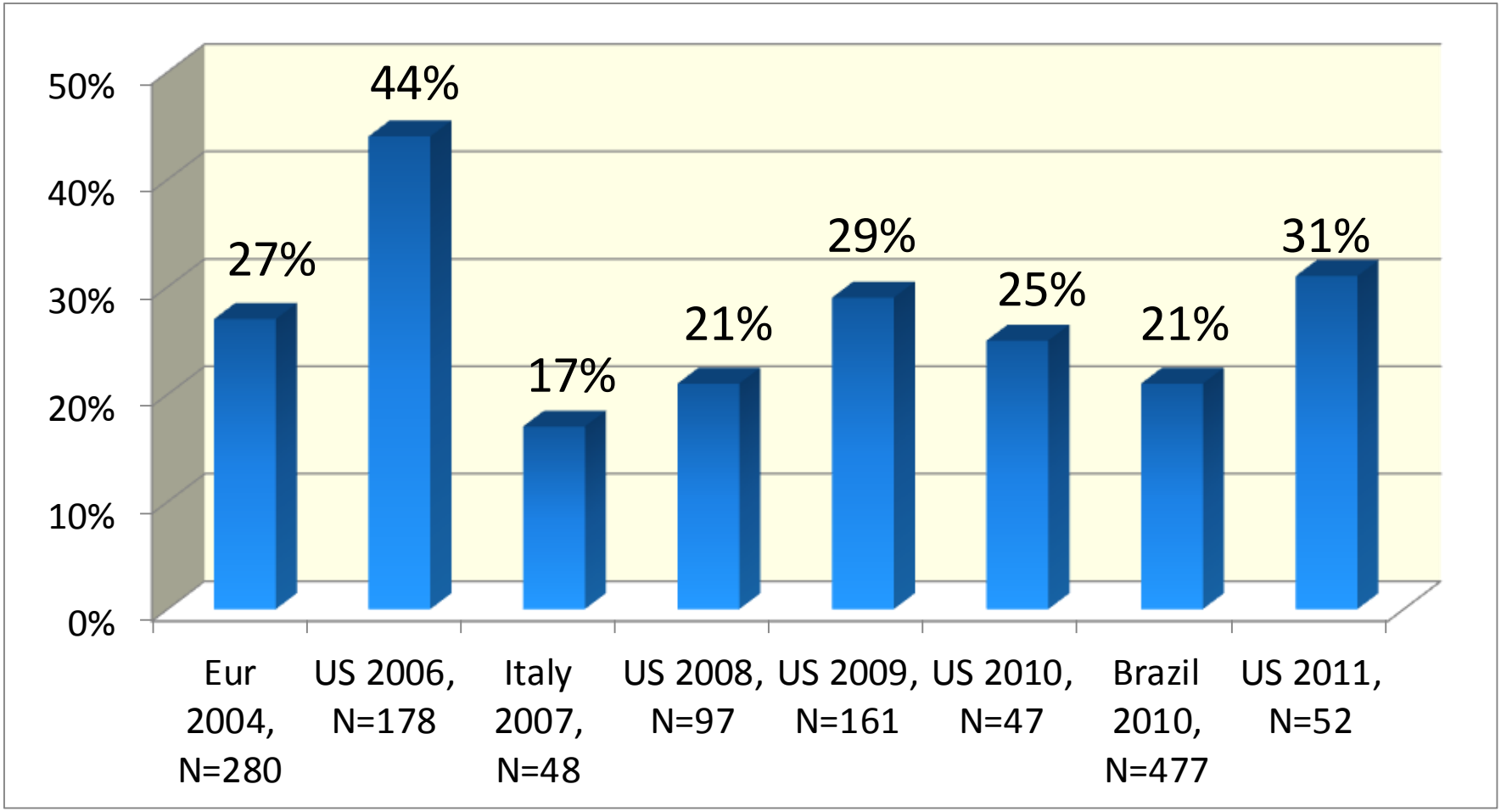
- Cardiovascular disease

- CNS dysfunction

- Behavioral challenges

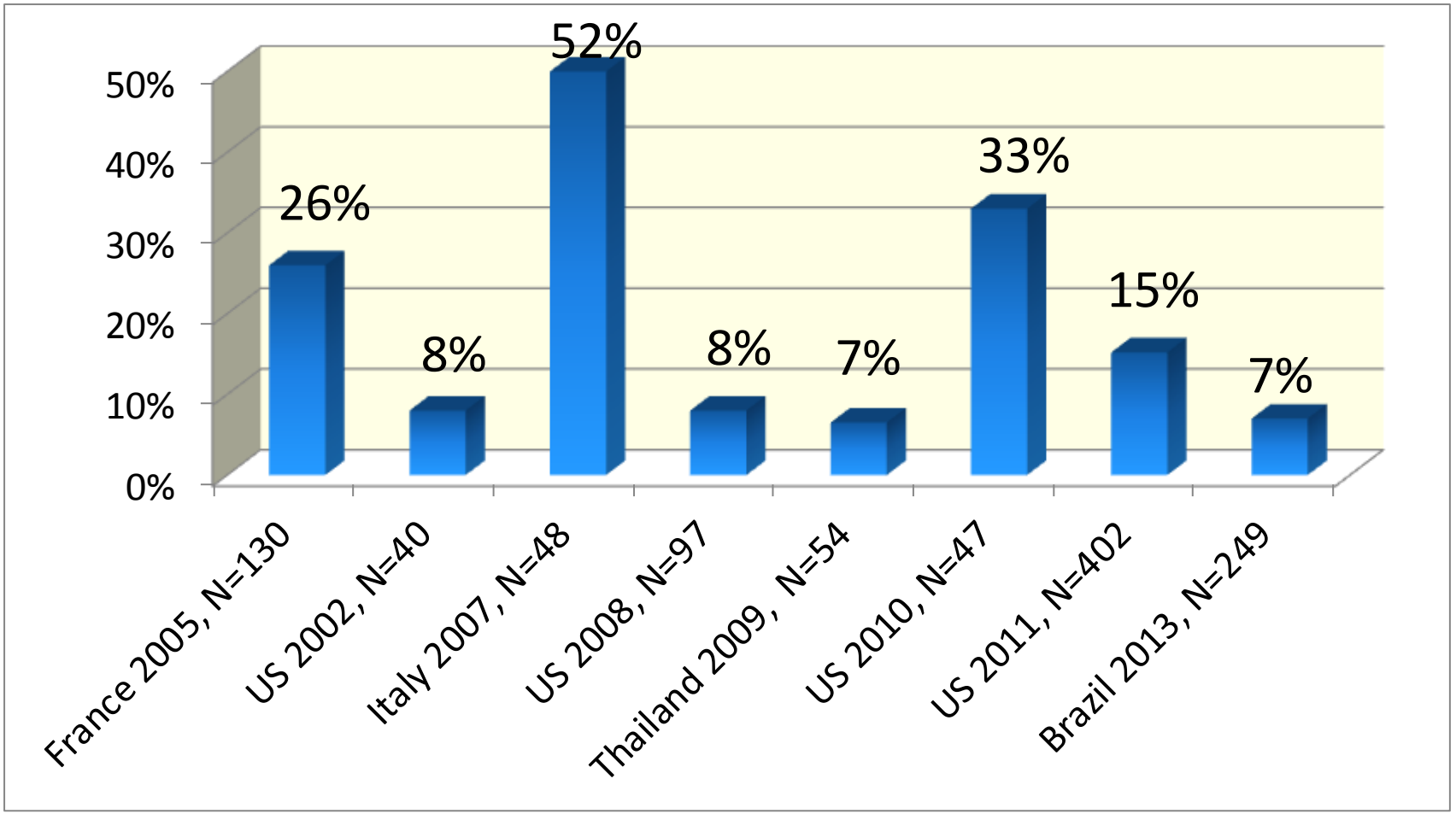
CARDIOVASCULAR HEALTH

Hypercholesterolemia Rates (>200mg/dL) in HIV-Infected Children



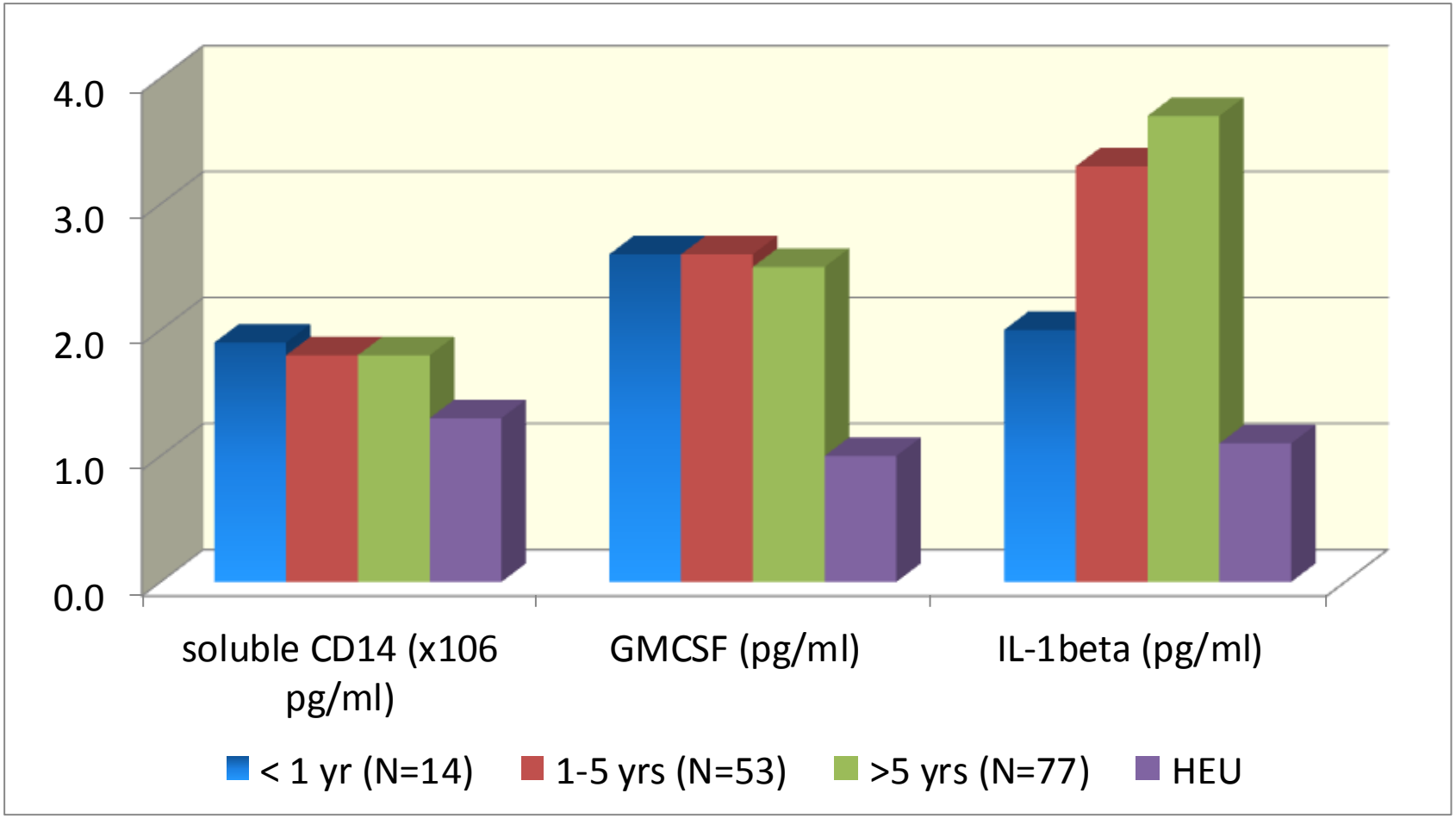
Euro Pediatr Lipodys Grp, *AIDS* 2004; Carter, *JAIDS*, 2006; Rosso, *Eur J Endocrinol* 2007; Chantry, *Pediatrics* 2008; Aldrovandi, *AIDS* 2009; Brewinski, *J Trop Pediatr*, 2010; Dimock, *Metabolism* 2010; Sztam, *J Pediatr Gastroentrol Nut,* 2011

Rates of Insulin Resistance in HIV-Infected Children



Beregszaszi, *JAIDS* 2005; Amaya, *PIDJ*, 2002; Rosso, *Eur J Endocrinol* 2007; Chantry, *Pediatrics* 2008; Lee, *HIV Med* 2009; Dimock, *Metabolism* 2010;Hazra, *PIDJ* 2013

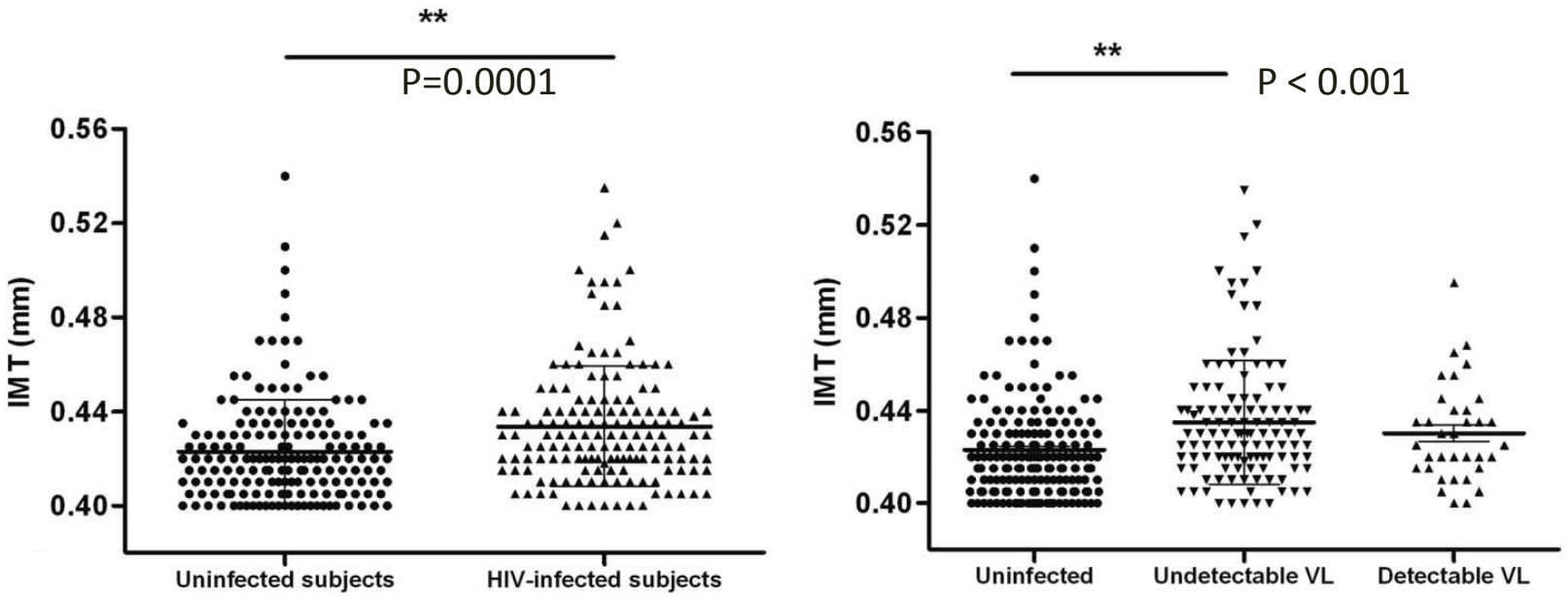
Sustained Elevation of Immune Activation Markers Regardless of Durable Long-term ART



P-value PHIV+ vs HEU:	<0.001	<0.001	0.004

Persaud, *JAMA Pediatr* 2014

Early evidence of cardiovascular disease: Carotid Intimal Media Thickness (cIMT)



- Measured carotid IMT in 150 HIV+ adolescents and 150 age- and sex-matched controls (age 14.6 years; 63% F)
- HIV: 97% perinatal; 97% on ART; 76% VL<50; 17% smokers
- IMT higher in HIV+ vs. HIV- overall and HIV w/VL < 50 vs. HIV-
- NO association of IMT with CRP or T cell activation/senescence

Sainz *JAIDS* 2013

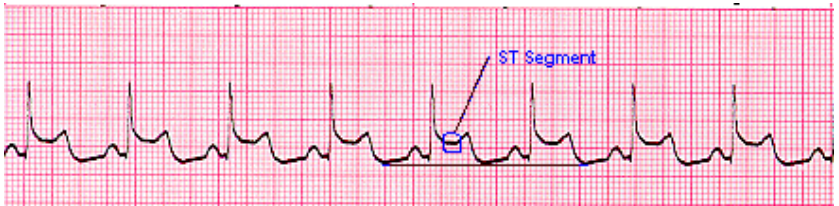
Pathobiological Determinants of Atherosclerosis in Youth (PDAY)

- Determined aggregate risk of cardiovascular disease among adolescents with perinatal HIV in the PHACS cohort using PDAY
  - Estimates risk of currently having atherosclerotic lesions in the coronary arteries or abdominal aorta
  - PDAY developed using autopsy data from over 1100 15-34 year olds
    - based on lipids, glucose, smoking, BP, and BMI
- In this cohort, 48% of HIV+ youth and 24% HIV- controls had scores > 0, indicating CVD risk
  - Higher risk among boys vs. girls

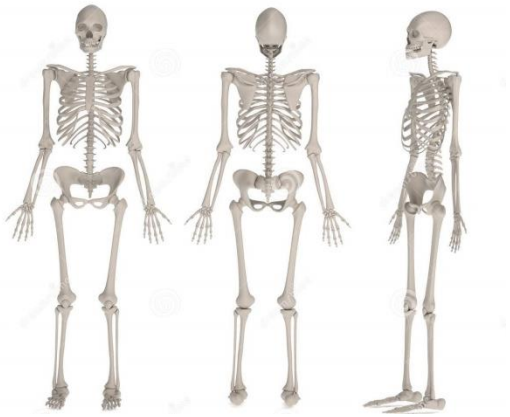
Patel, *Circulation* 2013

Findings suggest possible increased risk of CVD in adulthood

- Cardiovascular events are unusual in children & adolescents with perinatal HIV
- Emerging profile of lipid abnormalities, insulin resistance, elevated inflammatory and vascular markers
- These findings suggest possible increased risk of CVD in adulthood
  - *Will perinatal HIV with 1-2 decades of ART become an 'additional' risk factor for adult CVD or will it fade against more traditional CVD risk factors (smoking, obesity, etc.)*
- Risk reduction and monitoring should be routine part of HIV care



BONE HEALTH

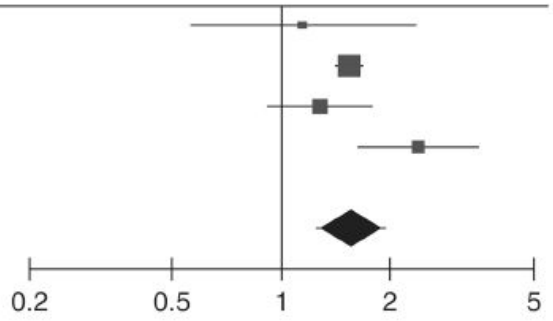


Evidence suggests an increased risk of fractures in adults with HIV infection

All fractures

Study	Weight	Incidence rate ratio 95% CI
Arnsten *et al.* 2007	9.0%	1.16 [0.57, 2.35]
Hansen *et al.* 2012	45.2%	1.55 [1.44, 1.68]
Yin *et al.* 2010	24.8%	1.28 [0.93, 1.78]
Young *et al.* 2011	21.1%	2.41 [1.64, 3.54]
Total (95% CI)	100.0%	1.58 [1.25, 2.00]

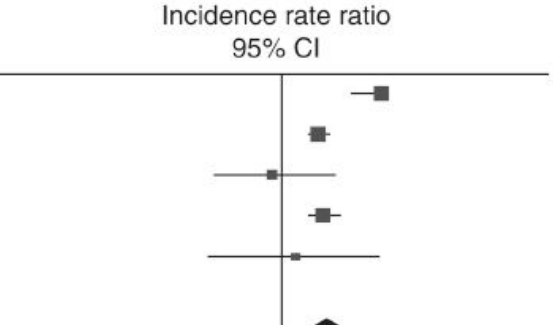
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 6.97$, df = 3 ($P = 0.07$); $I^2 = 57\%$
Test for overall effect: $Z = 3.80$ ($P = 0.0001$)



Fragility fractures

Study	Weight	Incidence rate ratio 95% CI
Hansen *et al.* 2012	25.1%	1.90 [1.70, 2.12]
Volk *et al.* 2011	26.5%	1.27 [1.20, 1.35]
Walker-Harris *et al.* 2012	13.8%	0.95 [0.65, 1.40]
Womack *et al.* 2011	25.5%	1.32 [1.19, 1.46]
Yin *et al.* 2010	9.2%	1.09 [0.64, 1.88]
Total (95% CI)	100.0%	1.35 [1.10, 1.65]

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 44.58$, df = 4 ($P = 0.00001$); $I^2 = 91\%$
Test for overall effect: $Z = 2.91$ ($P = 0.004$)

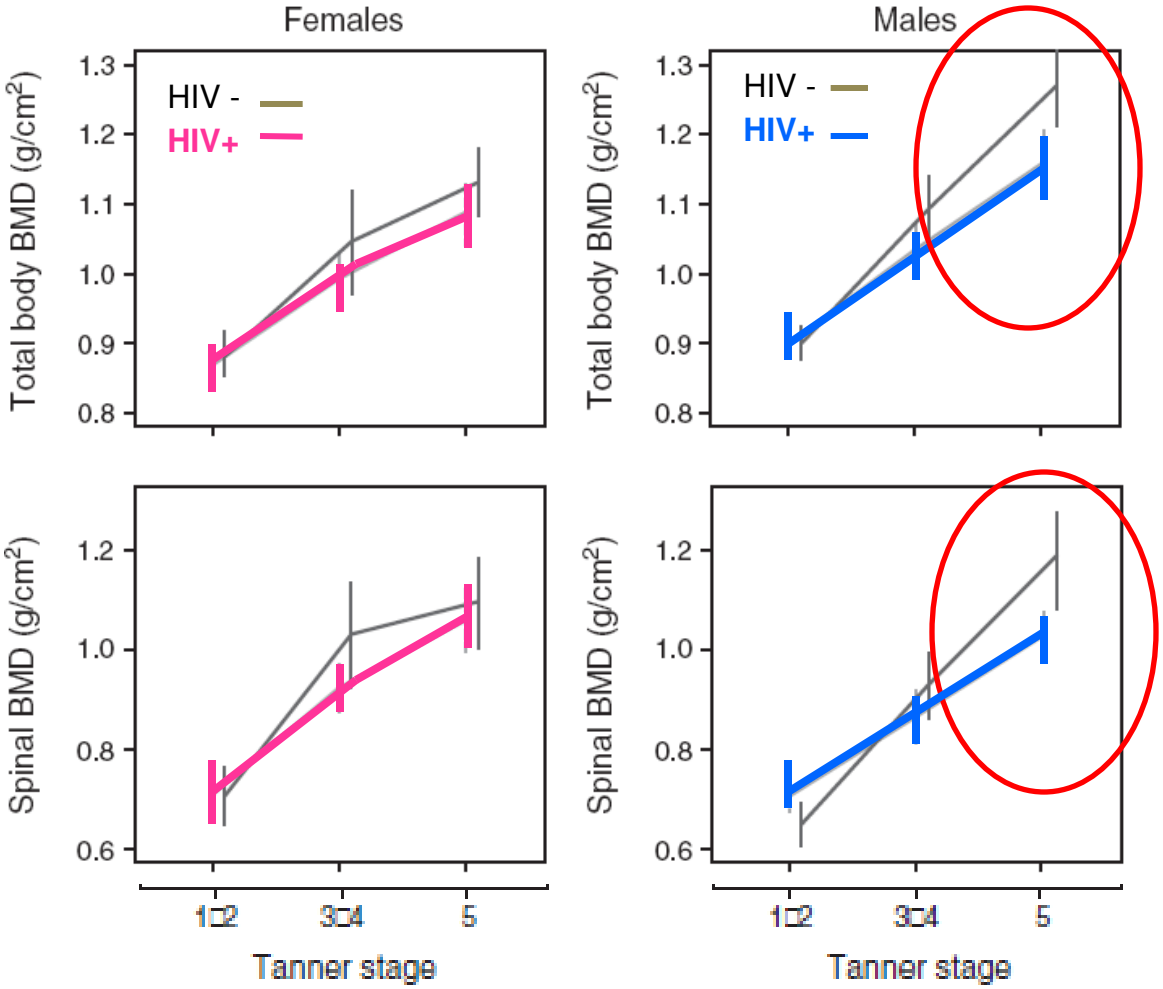


Shiau *AIDS*, 2013

Bone Mineral Density (BMD) through puberty

236 HIV-infected and 143 uninfected youth 7-24 years of age

Significant and widening differences between HIV+ and HIV- boys through puberty



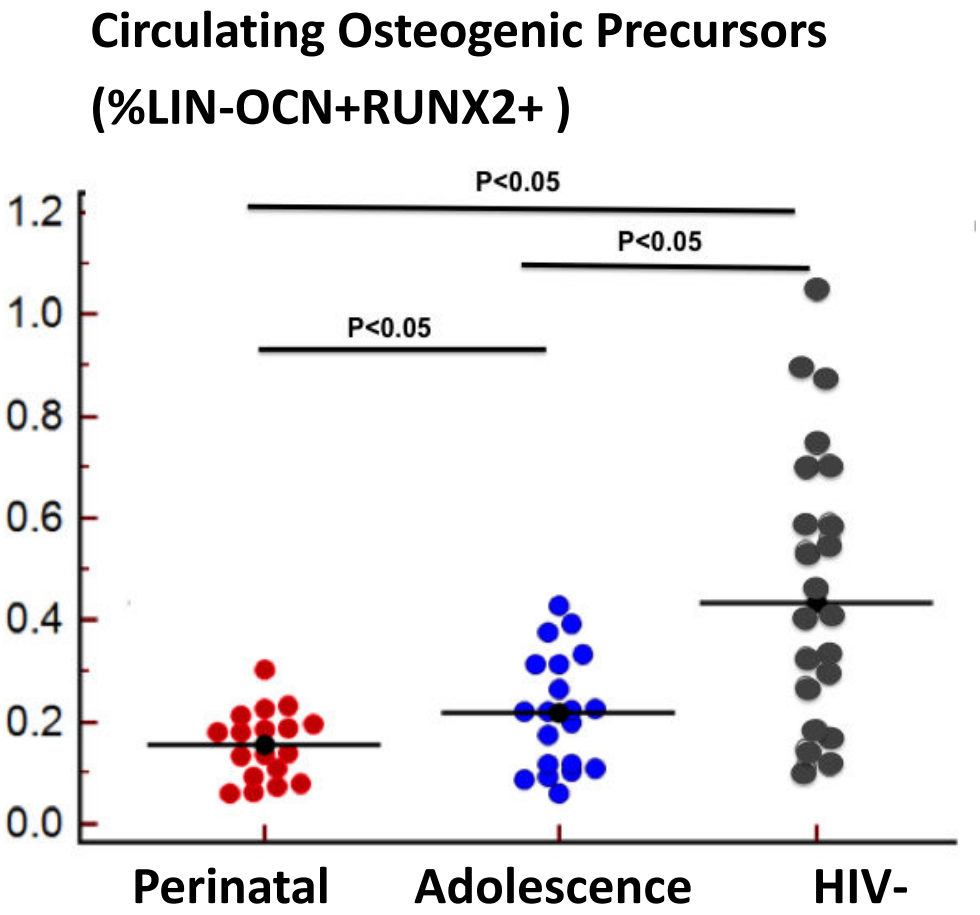
Jacobson D et al, AIDS 2010

Prevalence of low bone mineral density among HIV+ adolescents

Reference	Population	Duration of ART (years)	Findings	Associated factors
DiMeglio	$N = 350$ Mean age 12.6 years Black 66%, Hispanic 26% and white 8%	9.5 years (IQR 9.1–11.3) 25% had CDC C Nadir CD4 20%	Total body Z-score < -2.0; 7% versus 1% in HIV-negative peers LS Z-score < -2.0; 4% versus 1% in HIV-negative peers	Higher peak viral load and CD4% Ever used indinavir
Bunders	$N = 66$ Mean age 6.7 years Black 62%	3.4 years (IQR 1.5–5.2) 72% use PI, mainly nelfinavir	Spinal BMD Z-score $< -2.0 = 8\%$	
Puthanakit	$N = 100$ Age 14.3 years Thai 100%	7.0 years (4.3–8.7) Nadir CD4 = 114 (31–226) cell/mm3	LS Z-score < -2.0; 24%	Height-for-age Z-score < -1.5 Ever have WHO stage 4
Schtscherbyna	$N = 74$ Age 17.3 (SD 1.8) years White 36.5% Non-white 63.5%	11.1 years (SD 3.5) 91% on ART (19% NNRTI, 72% PI)	Low total body or lumbar spine in 32.4% of cohort Use of TDF is associated with lower lumbar spine Z-score: −1.8 (1.1) vs. −1.3 (0.9) Use of protease inhibitor is associated with LS Z-score −1.7 (1.1) vs. −1.1 (0.9)	Weight, BMI, nutrition, use of tenofovir and protease inhibitors

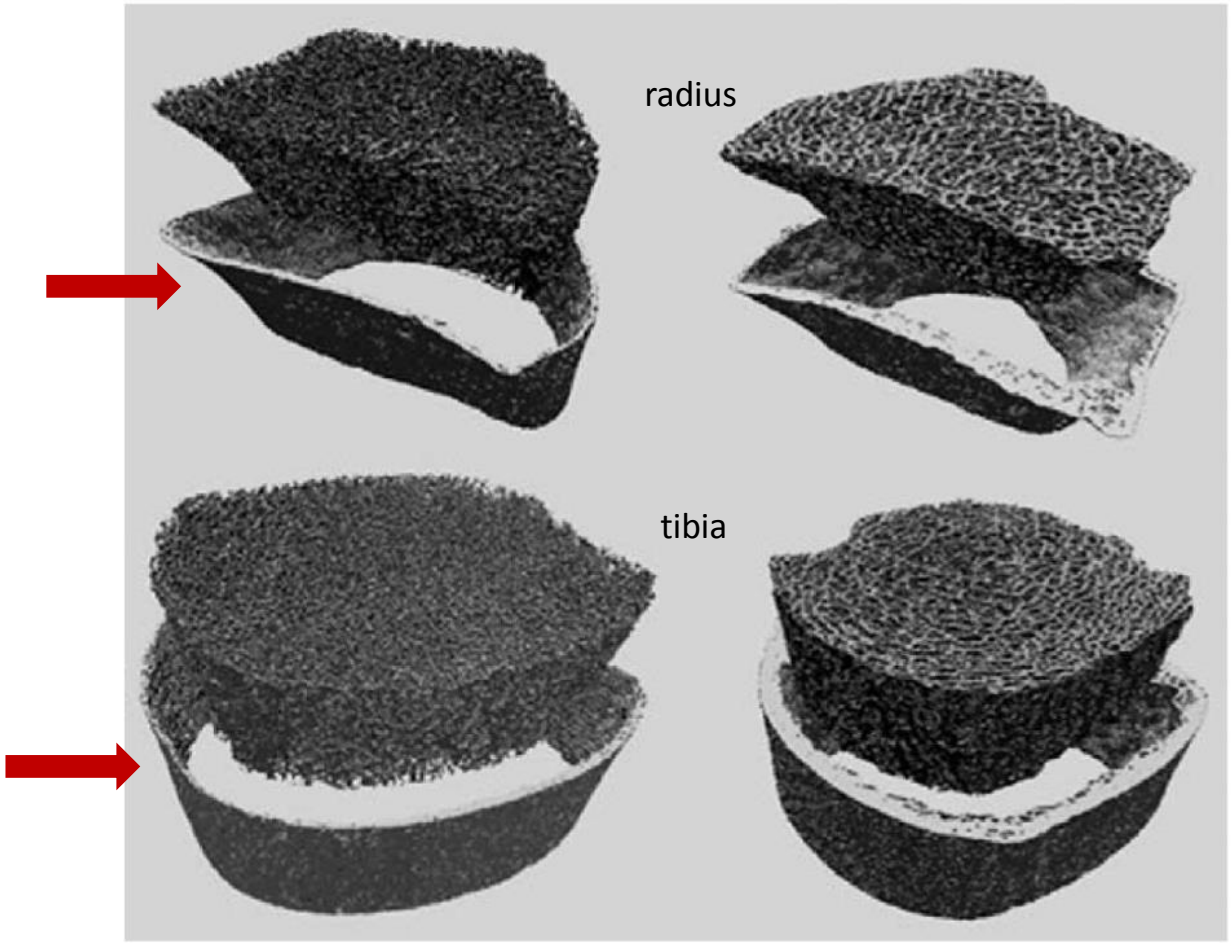
Puthanakit & Siberry, *JIAS*, 2013

Lower number of circulating osteogenic precursors in adolescents with perinatal HIV



Manavalan, CROI 2014, abstract #132

Lower peak bone mass and abnormal trabecular and cortical microarchitecture in young men infected with HIV early in life

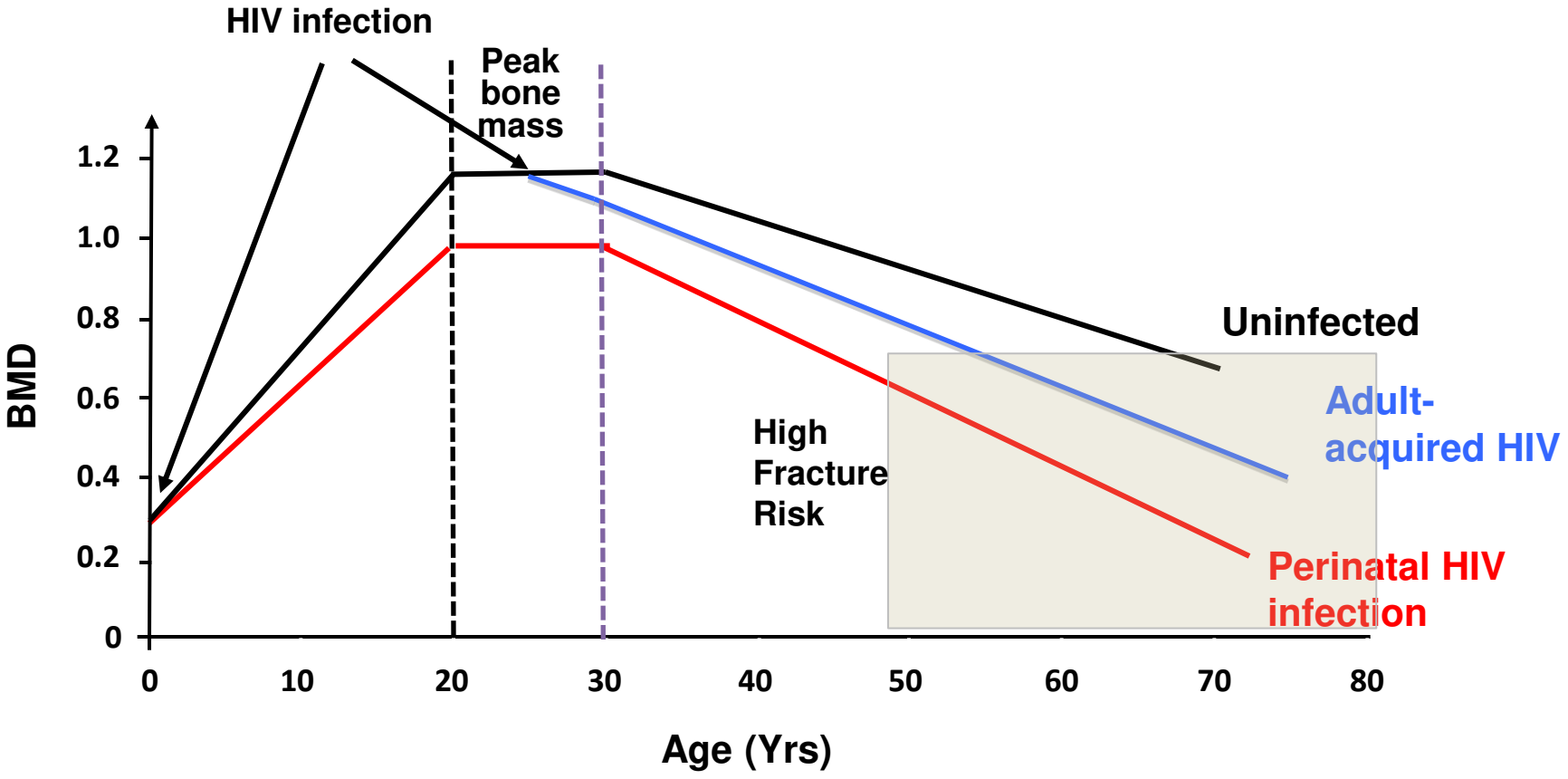


HIV+ 24-year-old man

HIV-24-year-old man

Yin, *AIDS* 2014

Does HIV infection early in life prevent attainment of a genetically-determined "peak bone mass"?



Adapted from Orwoll ES et al. *Endocr Rev*. 1995;16(1):87-116.

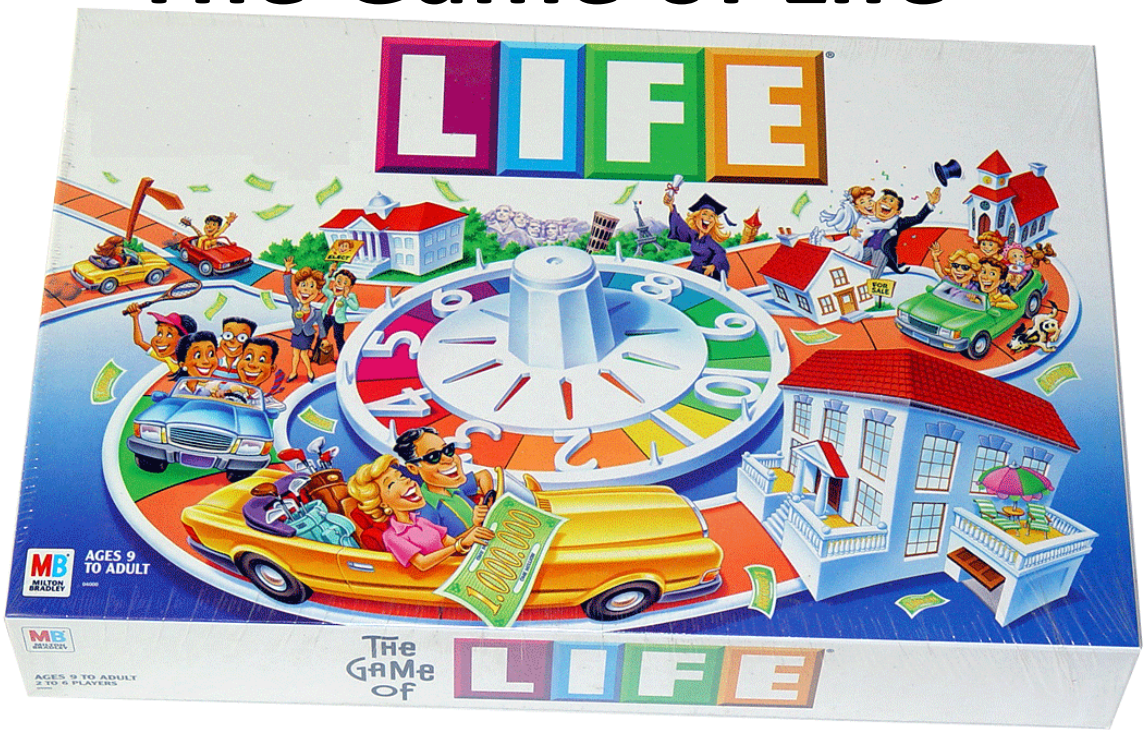
Prevention strategies to optimize bone health in perinatally HIV+ youth

Calcium + vitamin D	Ensure adequate intake of calcium (1300mg/day) and vitamin D (600IU/day) in adolescents
Promote healthy lifestyle	Good nutrition; avoid cigarette smoking; avoid/limit alcohol consumption
Exercise	Encourage high-intensity impact activities (running, jumping, gymnastics, basketball) for 10-20 min/day, 3days/wk
Effective ART	Regardless of regimen, ART that achieves virologic suppression, preserves/restores immunologic function should have positive effect on bone health
Avoid bone 'unfriendly' medications	Individualized risk-benefit assessment critical. Minimize use of systemic corticosteroids. For youth with multiple risk factors for poor bone health, consider avoiding TDF, boosed PIs, medroxyprogesterone

Puthanakit & Siberry, *JIAS*, 2013

PSYCHOSOCIAL AND BEHAVIORAL OUTCOMES

The Game of Life

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SALARY CARD
CAREER
STARTER HOME
HOUSE
Spin!
LIFE

Adolescence: transitioning from childhood to young adulthood

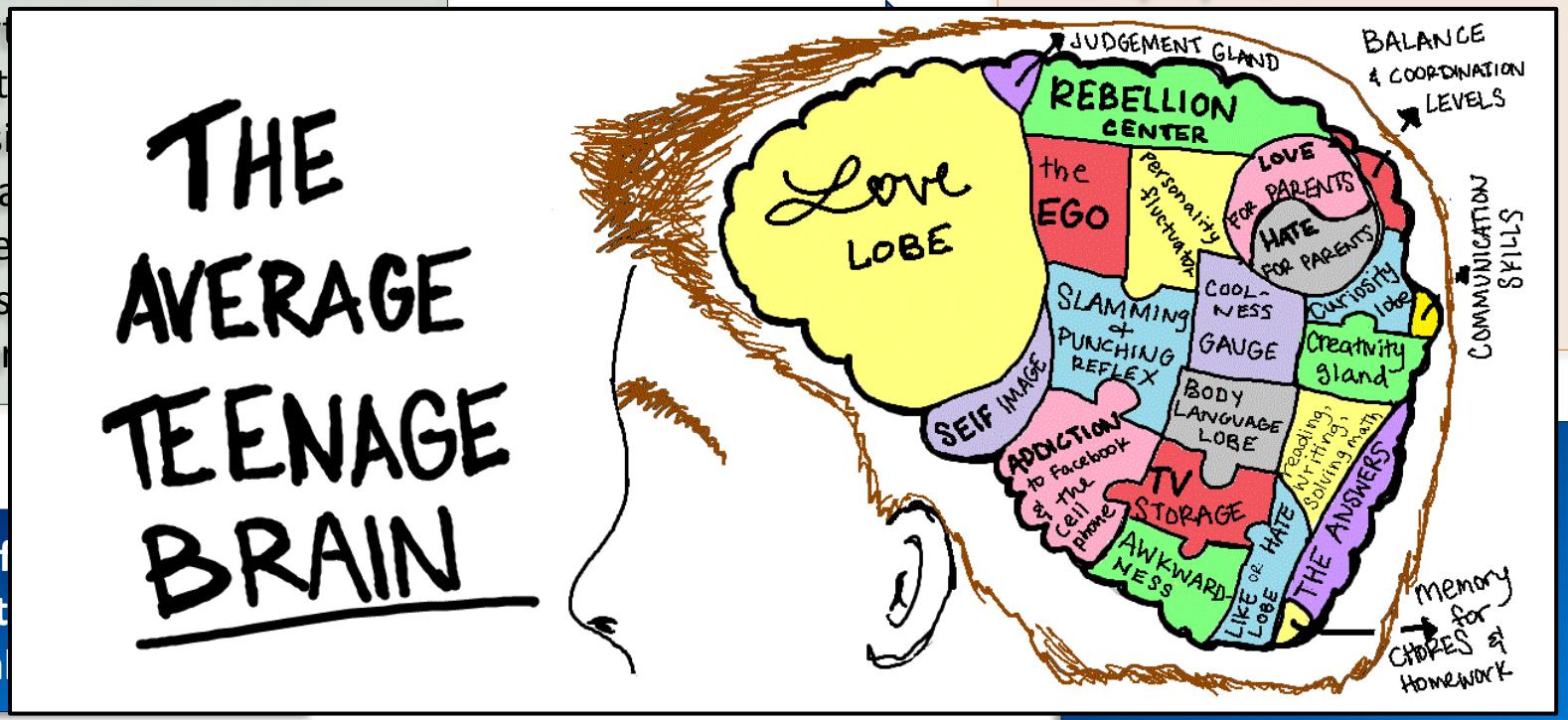
Childhood

- Dependence on parent/family/adults
- Physical and emotional growt
- Adult decisi
- Educa
- No se drugs
- Super

PERINATAL HIV INFECTION

Adulthood

- Independence
- Education complete
- Employment



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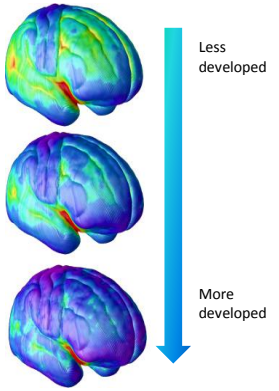
- Risk taking and experimentation

Risky behavior and adolescence
Blame it on the brain



- Increase in morbidity and mortality during adolescence associated with rise in risk behaviors:
  - Substance abuse, unprotected sex, antisocial acts, reckless & drunk driving
- Emerging data suggests risk-taking can be attributed to:
  - Immature/evolving neural system integration and efficiency, prefrontal cortex, limbic system, related structures
  - Limitations in executive function (cognitive processes associated with ability to carry out goal-directed behavior, impulse control, self-monitoring)
  - Personality traits of impulsivity, sensation-seeking, aggression and sociability were related to increased levels of risky behavior
  - **"The brain's inhibitory system does not match the demands of the excitatory or sensation-seeking systems, resulting in increased participation in risky behaviors."**

Pharo, *Behav Neurosci* 2011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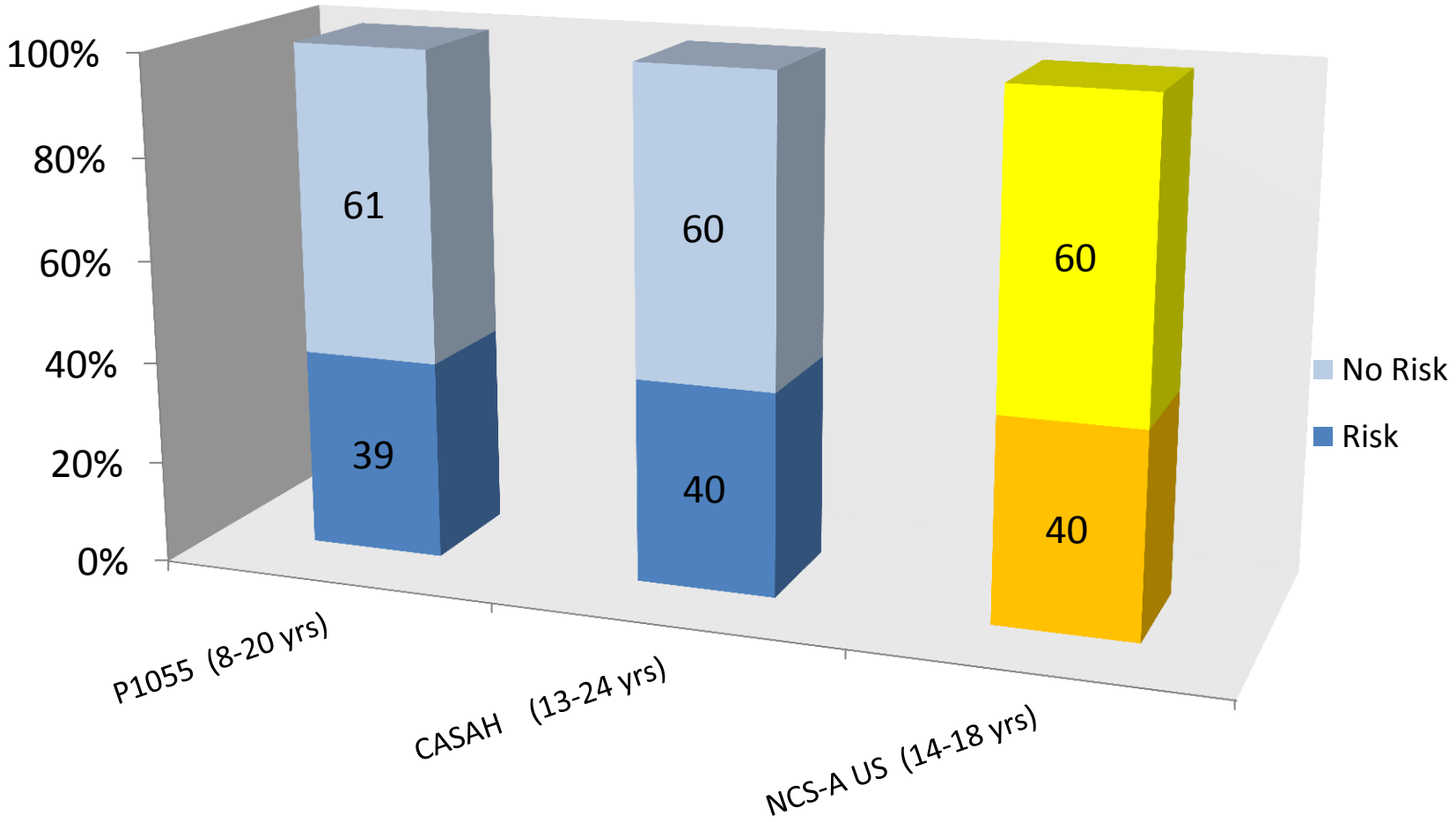
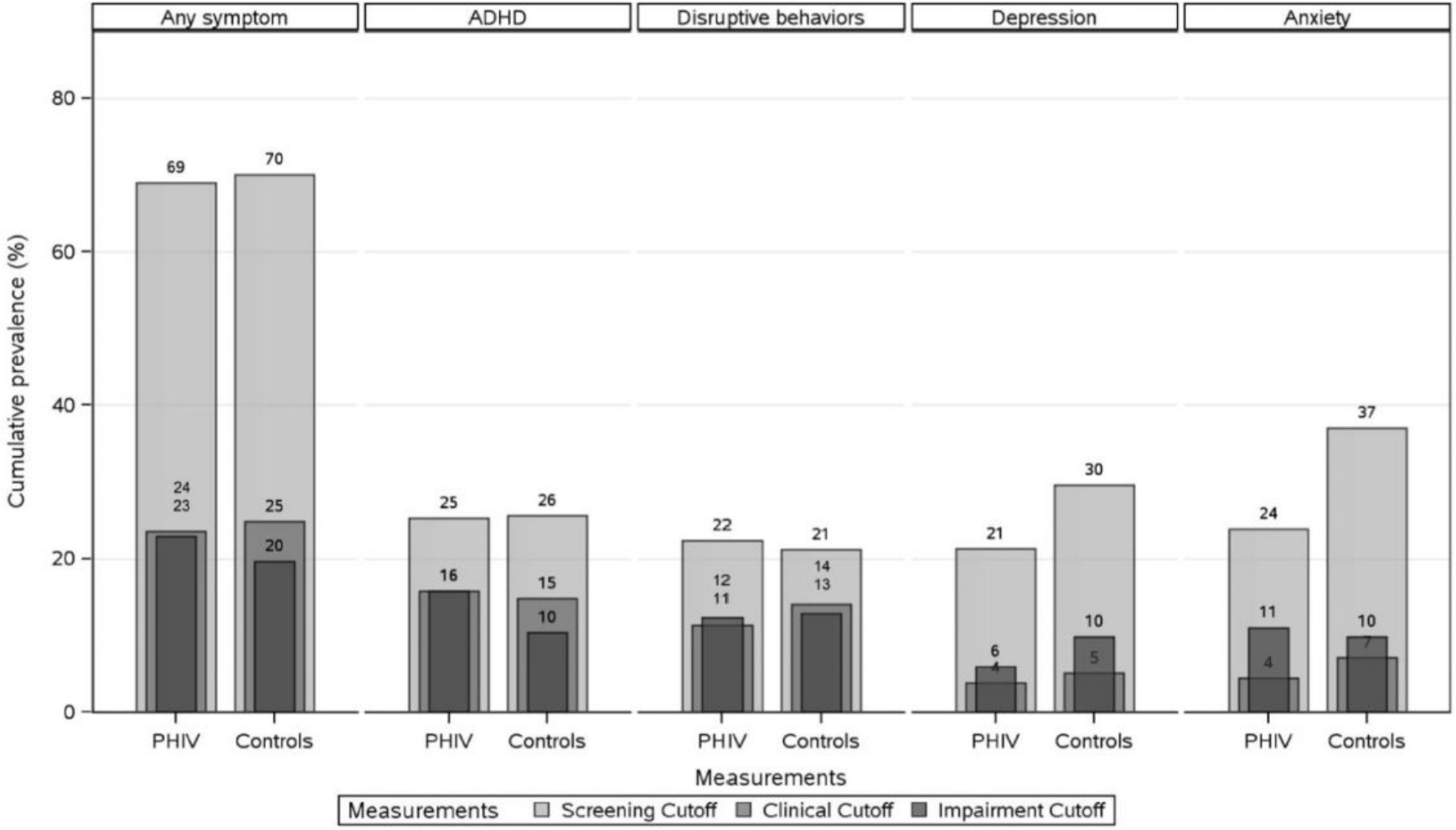
Spin!
LIFE

Psychiatric disorders among HIV+ youth



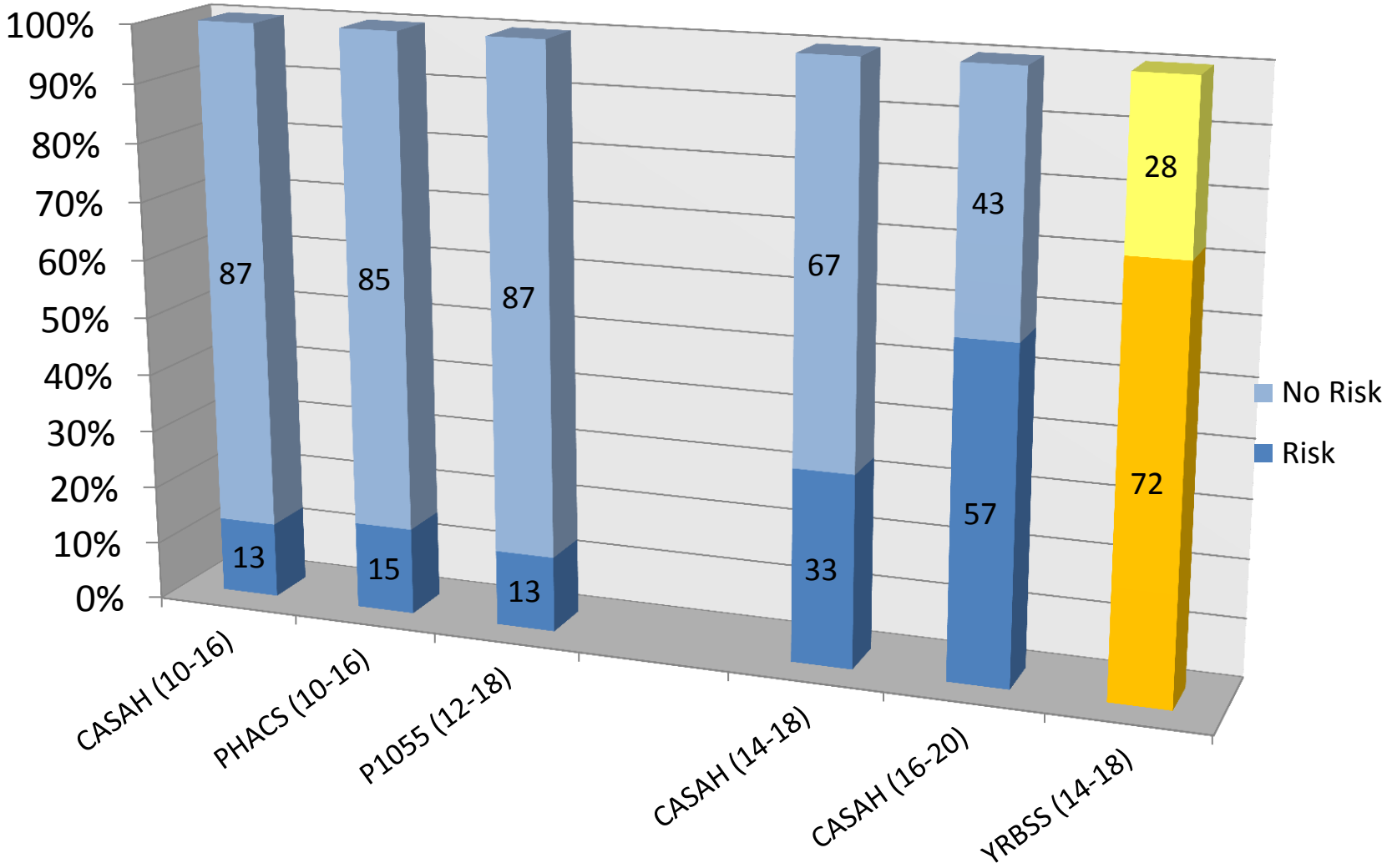
P1055 (Gadow, 2012); CASAH (Mellins, 2009, 2011); General Population (NCS-A, Kessler, 2012; n-10,148)

Psychiatric disorders among HIV+ and HIV-exposed & HIV-affected youth



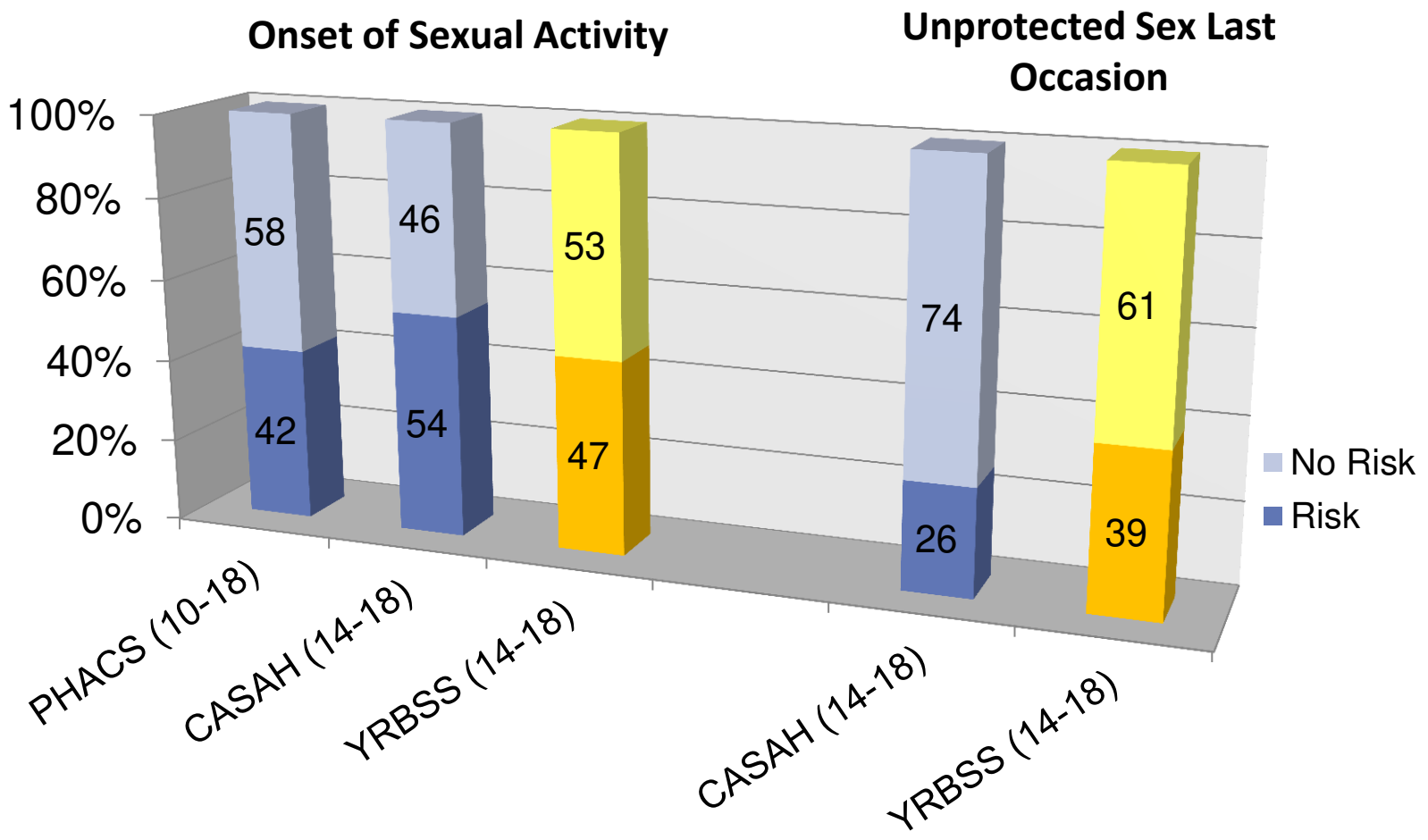
Gadow, *J Dev Behav Ped, 2010*

Substance use among HIV+ youth



P1055 (Williams, 2010); CASAH (Elkington, 2009); PHACS (Mellins, 2011); General Population (2009 Youth Risk Behavior Systems Survey; YRBSS; n-15,425)

Sexual risk among HIV+ youth



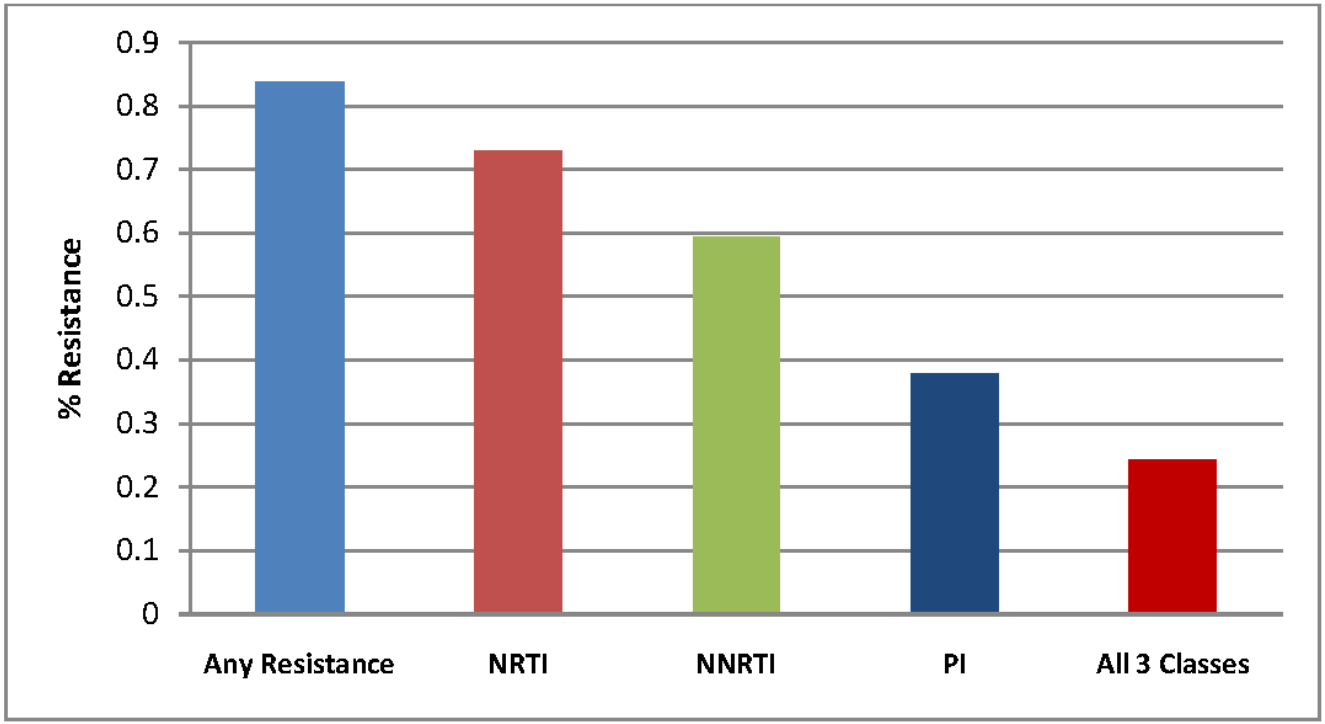
PHACS (Tassiopoulos, 2011; Mellins, 2011); CASAH (Bauermeister, 2009); General Population (2012 Youth Risk Behavior System Survey; YRBSS)

Sexual risk behavior increases over time and with substance use

- In the CASAH cohort, as expected, the proportion of youth who were sexually active increased with increasing age.
  - The odds of having unprotected sex was more than twice as great at each additional follow-up visit.
- The odds of engaging in unprotected sex over time were over 4 times greater if youth reported using alcohol (AOR 4.19; 95% CI [2.08, 8.44], $p < .001$) and twice as great if youth used marijuana (AOR = 2.29; 95% CI [1.05, 5.02], $p < .05$).

Elkington 2009, Bauermeiser, 2011

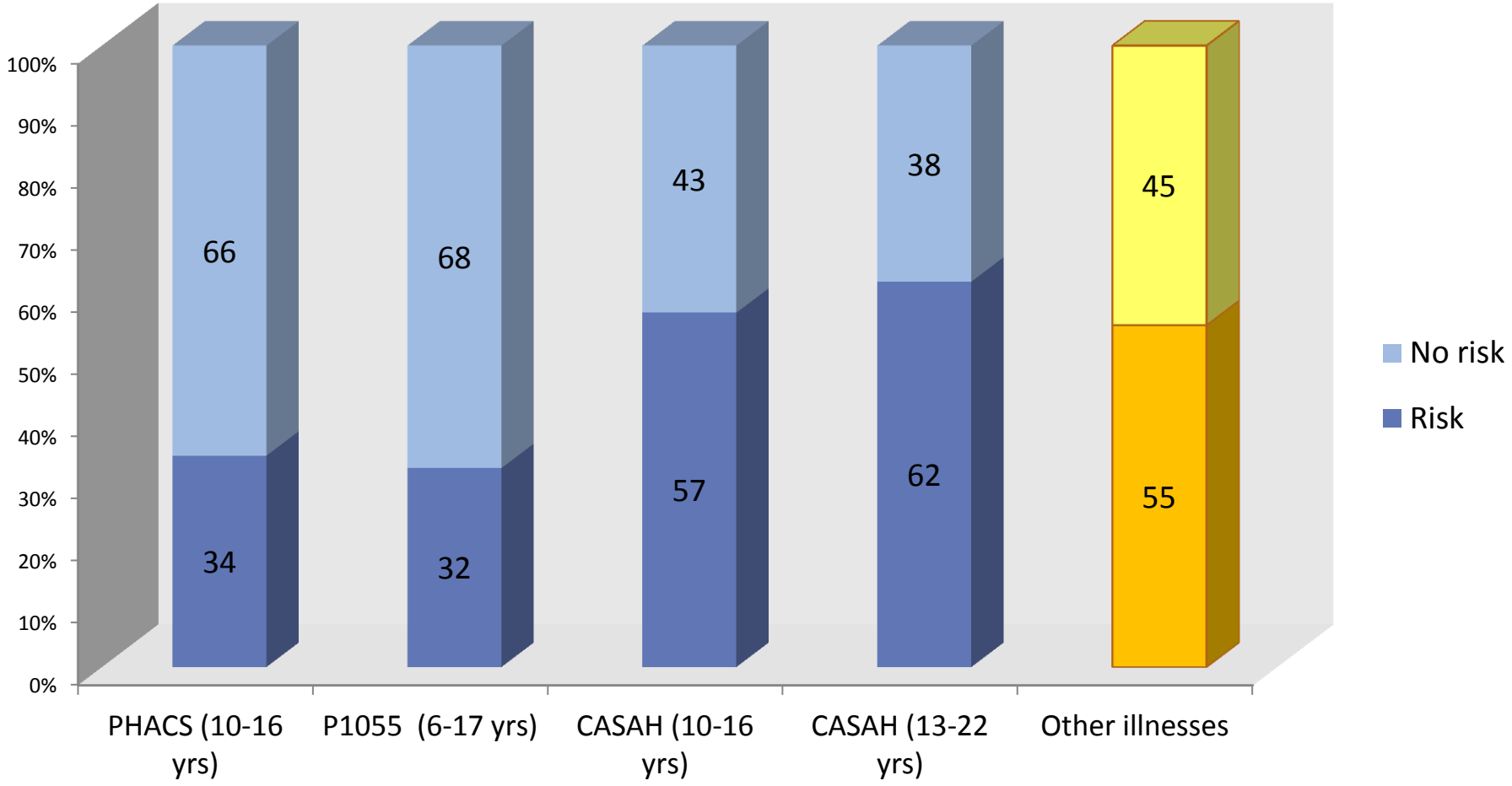
Viral resistance in sexually active youth with HIV RNA>5000 copies/ml (n=38), PHACS



- 42% of 92 sexually active ≥1 VL >5000 copies/ml
- 81 % had resistance to ≥1 ARV class
- 24% had some resistance to drugs in all 3 classes
- 63% with resistance reported unprotected sex

Tassiopoulos et al. (2013)

Reported non-adherence in the last month among HIV+ youth



PHACS (Mellins, 2011; Usitalo, 2009); CASAH (Marhefka, 2009); P1055 (personal communication, Kacanek, 2013); Other illnesses (Bender, 2000; Johnson, 2002)

Systematic review and meta-analysis of ART adherence in adolescents

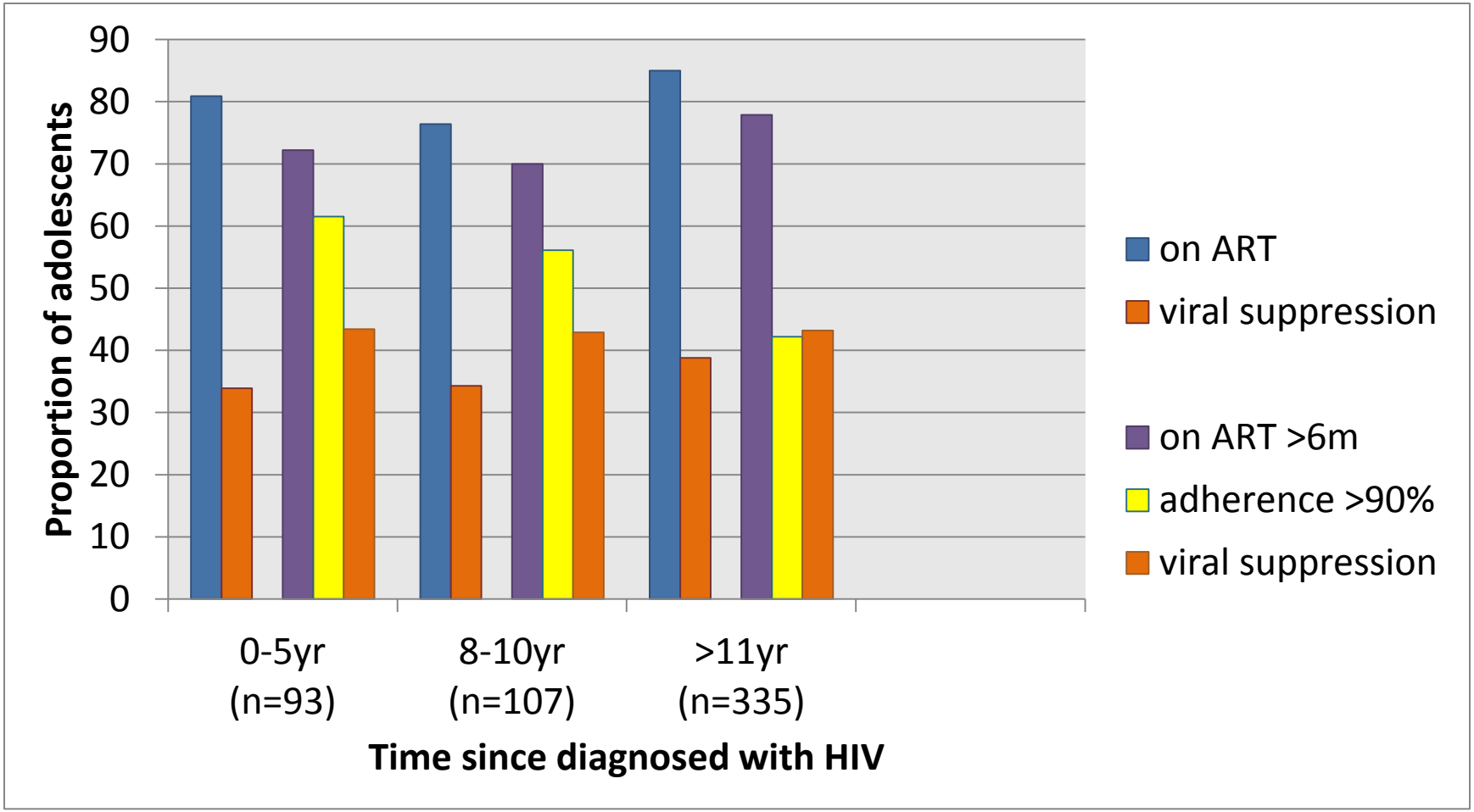
	Number of studies	% adherence	95% CI
Overall	50	62.3	57.1–67.6
North America	22	52.7	46.5–59.0
Africa	8	83.8	78.9–88.7
Asia	3	83.9	76.8–91.0
Europe	12	62.0	50.7–73.3
South America	5	62.8	46.6–77.0
Sex			
≥50% female	27	65.6	58.8–72.4
<50% female	15	54.3	45.9–62.7
Age			
Adolescents [12–29]	34	60.1	53.3–67.0
Young adults [20–24]	10	67.9	58.6–77.3
Study year			
Before 2005	22	59.3	49.2–69.4
2005 onwards	16	77.0	72.0–82.0
Adherence measure[a]			
Viral load	36	62.2	56.0–68.4
Self-report	20	59.1	51.8–66.4

Kim, AIDS 2014

Challenges of adherence accentuated during adolescence

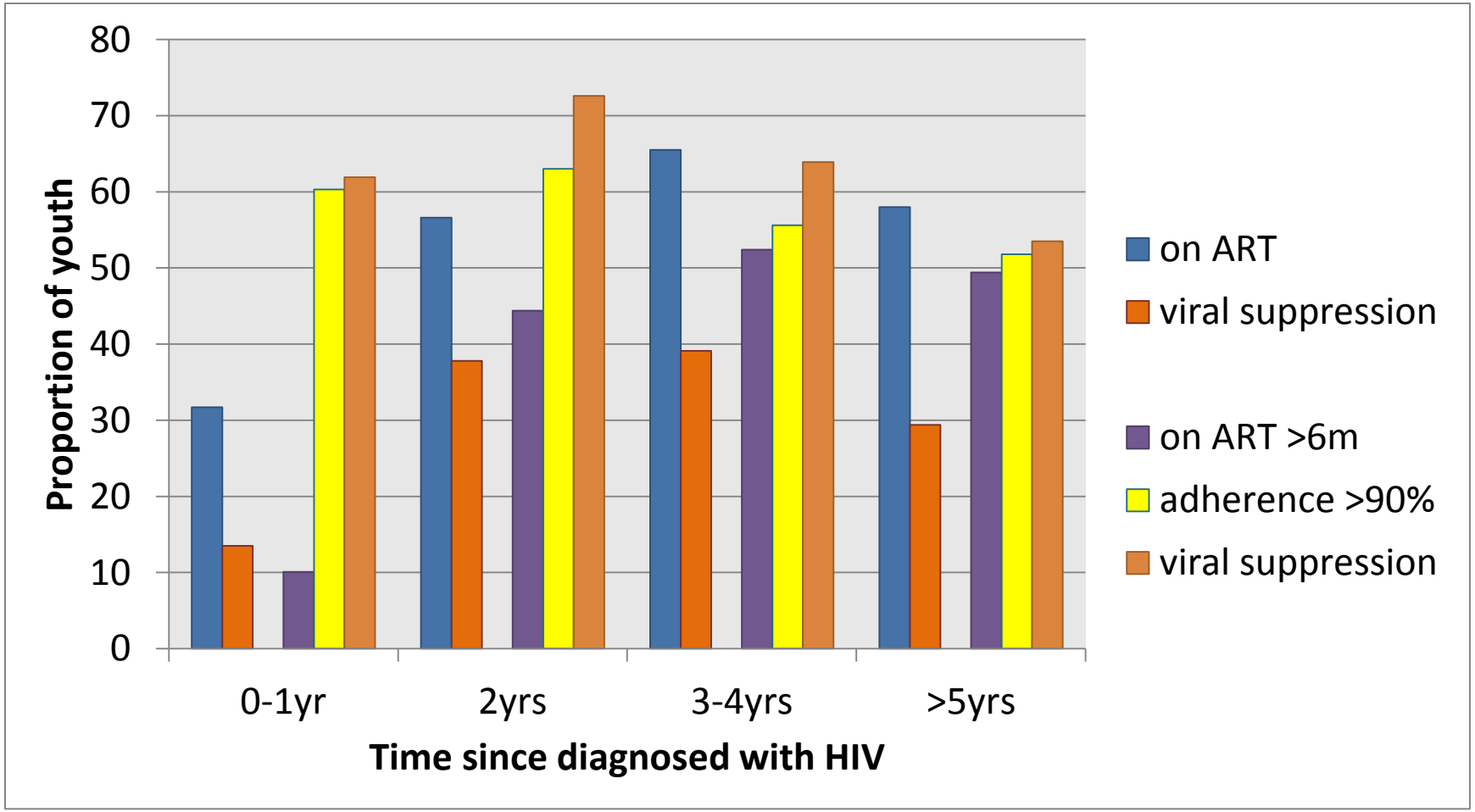
- Barriers to adherence cited by adolescents: forgetting, not wanting to be reminded about HIV, not wanting to take medications
  - Drug holidays (unplanned ART interruptions) not uncommon
- Few interventions have been demonstrated to improve adolescent adherence
  - Suggested benefit of adherence support devices (such as medication boxes and beepers), cell phone support, and offering individual and group support and motivational interviewing
- Adolescent perspectives imply importance of: improving knowledge, better, long-acting formulat additional adherence support, earlier disclosure

Rates of viral suppression among 649 perinatally infected youth, US



Kahana, JAIDS, 2015

Rates of viral suppression among 1547 youth with behaviorally acquired HIV, US



Kahana, JAIDS, 2015

ART exposure among adolescents with perinatal infection

- Oldest youth are often highly drug experienced with history of sequential monotherapy, non-suppressive regimens, inadequate adherence and MDR HIV
- Among younger youth there is generally less historic drug exposure having initiated ART with more potent, forgiving and tolerable regimens
- Adolescents, unlike young children, are often able to benefit from introduction of new drug classes and simplified regimens approved for adult therapy
  - Few meaningful pharmacologic/dosing differences
  - Lingering concerns re: toxicities during puberty
  - Each new 'drug' saves a few more adolescents who burned through existing options
  - *Still have to take a pill at least once daily*

Genotype of 17 year old with perinatal HIV, NYC

PI Major Resistance Mutations:	**G48V, I54V, V82A, I84V**
PI Minor Resistance Mutations:	**L10I, V11I, Q58E, A71V**
Other Mutations:	I13V, M36I, L63P, N83S

Protease Inhibitors

atazanavir/r (ATV/r)	High-level resistance
darunavir/r (DRV/r)	Low-level resistance
fosamprenavir/r (FPV/r)	High-level resistance
indinavir/r (IDV/r)	High-level resistance
lopinavir/r (LPV/r)	High-level resistance
nelfinavir (NFV)	High-level resistance
saquinavir/r (SQV/r)	High-level resistance
tipranavir/r (TPV/r)	High-level resistance

NRTI Resistance Mutations:	**M41L, D67N, T69G, L74V, L210W, T215Y, K219R**
NNRTI Resistance Mutations:	**V108I, E138Q, Y181C**
Other Mutations:	None

Nucleoside RTI

lamivudine (3TC)	Low-level resistance
abacavir (ABC)	High-level resistance
zidovudine (AZT)	High-level resistance
stavudine (D4T)	High-level resistance
didanosine (DDI)	High-level resistance
emtricitabine (FTC)	Low-level resistance
tenofovir (TDF)	High-level resistance

Non-Nucleoside RTI

efavirenz (EFV)	Intermediate resistance
etravirine (ETR)	Intermediate resistance
nevirapine (NVP)	High-level resistance
rilpivirine (RPV)	Intermediate resistance

Drug resistance mutations among adolescents transitioning to adult services

- 112 adolescents transferring to adult HIV care services underwent genotypic analysis
- 63/112 had genotypes available
  - 5 ART-naive (no primary mutations)
  - 58 ART-experienced
- Median duration of ART: 13.5y
- Drug resistance:
  - 51% PI mutations
  - 77% NRTI mutations
  - 37% NNRTI mutations

De Mulder, *PLOS ONE* 2012

Lifetime adherence to ART – are we asking the impossible?

- Adherence is a formidable challenge for adolescents
  - Highly vulnerable to normal adolescent developmental
- Challenges of daily medication administration are accentuated during adolescence
- Adherence is not static: good today, gone tomorrow
- No perfect (and few good) measures of adherence
- Many are studying approaches to optimize ART adherence

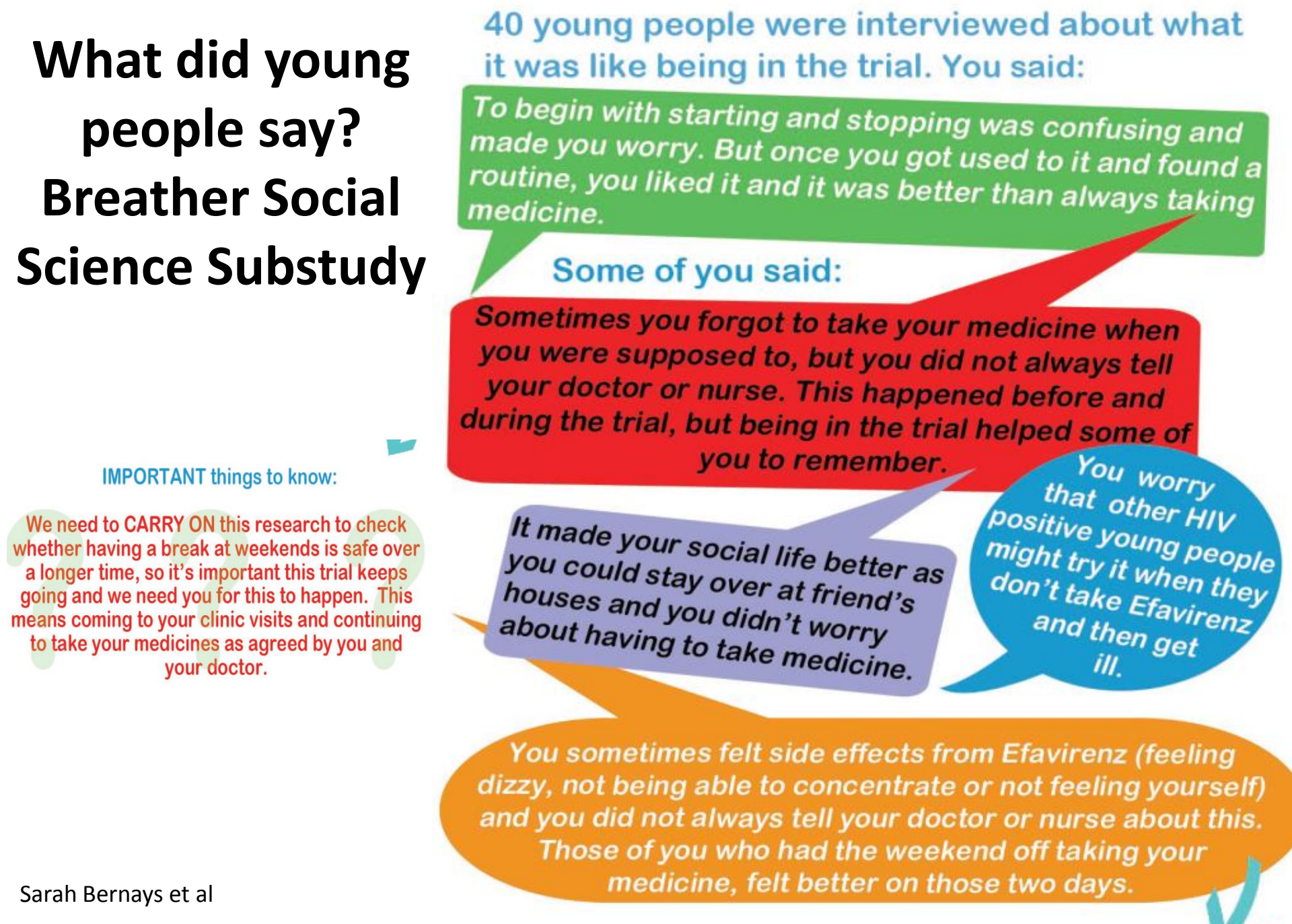
BREATHER (PENTA 16)

Randomised 48week trial of weekend breaks in viral load suppressed young people 8-24 years on efavirenz

- **Non-inferiority of VL suppression in young people on EFV-based 1st line ART was demonstrated for Short Cycle therapy (weekend breaks) vs. Continuous therapy**
- **2-year follow-up as randomized continuing**

Butler K. 38LB CROI 2015

What did young people say? Breather Social Science Substudy



Sarah Bernays et al

Case Study

I have an adolescent, very smart, meth addicted, patient … she seems to genuinely want to take his meds, but just goes on benders and forgets. I asked him, "If had an injectable form of the medicines that you get once a month or every other month instead of taking pills, would that interest you? She said "ABSOLUTELY" … when I asked if the pain of the shots would be a deterrent. She said definitely not, shoots up, no fears about needles, etc … but then, fast forward 10 minutes later into our visit, we move to one of his next problems … early latent syphilis. To this she says, "no way, if you make me get it , I am leaving right now, is there anything we can do by pill?" … so I call her on it, I say, you just told me that shots aren't a problem? "yes but that one hurts a lot" … After several minutes of my trying to convince her about PCN, I concede to doxy BID. She tries for 3 days, gets too much GI upset, comes in a gets PCN IM.

Ted Ruel, UCSF

SEXUAL AND REPRODUCTIVE HEALTH

Pregnancy in perinatally-infected females

- Between1998-2013, 16 publications on 277 pregnancies in 231 perinatally-infected girls.

Author/Journal	Year (place)	# Perinatal Girls	# Pregnancies	# Infected
Crane Ob/Gyn	1998 (Boston)	Case rpt: 1	1	0
CDC MMWR	2003 (Puerto Rico)	Case rpt: 8	10	0/7 live birth
Chibber Arch Gyn/Ob	2005 (India)	Case rpt: 30	30	0/26 live birth
Bernstein J Adol Health	2006 (Wash DC)	Cohort: 6/43 (14%)	6	Unk
Ezeanolue J Adol Health	2006 (Newark)	Cohort: 5/28 (18%)	5	Unk
Levine J Adol Health	2006 (Philadelphia)	Case rpt: 2	2	0
Brogley Am J Pub Health	2007 (US)	Cohort: 38/638 (6%)	45	1/32 live birth
Koenig Am J Ob/Gyn	2007 (US)	Case rpt: 15	15	Unk
Thorne AIDS	2007 (Europe)	Case rpt: 9	11	0/8 live birth
Meloni AIDS Care	2009 (Italy)	Case rpt: 2	2	0
Williams Am J Ob/Gyn	2009 (Newark)	Case rpt: 10	13	1/7 live birth
Kenny J HIV Med	2012 (UK/Ireland)	Cohort: 30/252 (12%)	42	0/3 live birth
Jao AIDS	2012 (NYC)	Case rpt: 14	17	0/17 live birth
Millery J Ass Nurs AIDS Care	2012 (NYC)	Cohort: 25/97 (26%)	33	0/19 live birth
Croucher Sex Trans Inf	2013 (UK)	Cohort: 6/31 (19%)	8	0/3 live birth
Munjal Adol Health Med Th	2013 (Bronx)	Case rpt: 30	37	1/37 live birth

Pregnancy in perinatally-infect[illegible]ales

- Between1998-2013, 16 pu[illegible]1 perinatall[illegible]

Autho[illegible]				ted
Crane				
CDC M[illegible]				rth
Chibber[illegible]				rth
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Levine J A[illegible]				
Brogley An[illegible]				
Koenig Am J[illegible]				
Thorne AIDS				
Meloni AIDS				
Williams Am J[illegible]				
Kenny J HIV M[illegible]				live birth
Jao AIDS			17	0/17 live birth
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Munjal Adol Health Med Th	2013 (Bronx)	Case rpt: 30	37	1/37 live birth

- Majority of pregnancies were unplanned.
- Elective termination was not uncommon (15%-42% in 5 studies reporting).
- Repeat pregnancy was not uncommon: 32 had 2 pregnancies; 4 had three pregnancies.
- Adverse pregnancy outcomes: miscarriage (6-14% 4 studies), preterm (7-44% 4 studies),SGA (47% 1 study), low birth weight (1 study).
- MTCT uncommon (3 infections/159 live birth, 2%)

Pregnancy in perinatally-infected adolescents in the UK

759 females born before 2001
44(6%) have had at least 1 pregnancy, 19 had 2 pregnancies, 4 had 3 or 4 pregnancies
9 terminations, 2 miscarriages, 51 live births, 5 continuing to term
Median age at conception was 19 years
36% with CD4 >500; 15% CD4 350-499; 49% CD4 <350
71% were on ART at conception
VL at delivery <50 copies/mL in 64% , 51-1000 in 31% and >1000 in 5%.
44% delivered by elective CS, 27% by emergency CS, 27% by planned vaginal delivery and with one unplanned vaginal delivery

Byrne *JIAS*, 2014

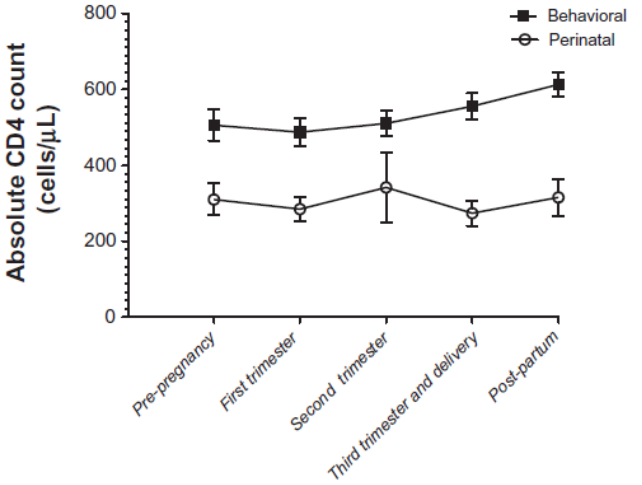
Complex health profile of pregnant women with perinatal infection

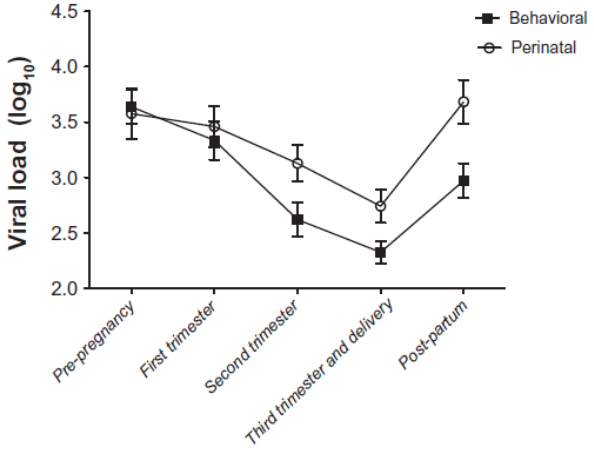
	Women with perinatal HIV (n=16)		Women with behaviorally acquired HIV (n=60)	
Age (yrs)	20 (19-23)		30 (23-37)	
Substance use				
Prior to pregnancy	6	43%	31	52%
During pregnancy	1	7%	10	17%
Hx of OI	6	43%	6	10%
Nadir CD4 during pregnancy (cells/mm	231 (38-374)		391 (286-544)	
Nadir CD4 ≤200 during pregnancy	9	64%	5	16%
Viral suppression at delivery	10	71%	52	87%
Second line ART	6	43%	0	0
SGA infant	8	47%	12	12%

Jao *AIDS* 2013

Impact of HIV infection on pregnancy and maternal health

- All pregnancies at two Bronx, NY hospitals (37pregnancies to 30 PHIV, 40 pregnancies in 35BHIV) through 1 year postpartum period
- Followed 10 PHIV and 21 BHIV women for 4 more years. Mortality outcomes:
  - No deaths BHIV
  - 4 deaths (13%) in the PHIV with complications of HIV: 3 with CD4 < 50 cells/µL and VL log10 > 4.7 copies/mL at 1yr postpartum.



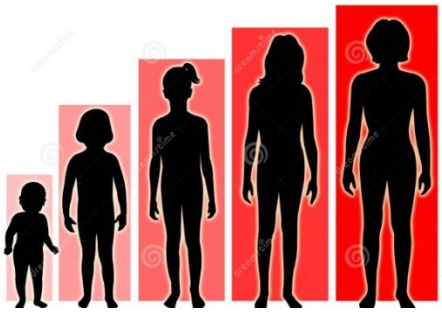


Munjal *Adolescent Health, 2013*

TRANSITION

Meeting the needs of adolescents living with HIV infection

- Generally children with perinatal HIV infection have received lifelong care in pediatric settings
  - Dedicated child-focused, comprehensive HIV service programs with pediatric care specialists and multidisciplinary teams
- Increasingly large numbers are aging into adolescence, a stage of great risk and resiliency
- Biomedical and psychosocial legacy of HIV infection necessitate specific services
  - Reproductive and sexual health needs



Talking about 'transition'… What exactly do we mean?

- It is not uncommon for pediatric programs to expand service delivery to meet needs of the growing adolescent population
  - Expansion often organic and unplanned
- Many programs are simultaneously exploring how best to transition youth to adult service programs
  - *Transition is defined as a purposeful process that addresses the medical, psychological and educational/vocational needs of adolescents and young adults with chronic physical and medical conditions as they move from child-centered to adult-oriented health care systems* *(National Service Framework www.dh.gov.uk/publications)*
  - *Transition is the purposeful and planned movement of adolescents from child-centered to adult-oriented services (http://apps.who.int/adolescent/hiv-testing-treatment/page/Transition)*
  - *Transition is the process that maximizes resiliency, minimizes risks, promotes personal growth and strengthens the ability to self-manage*

What do we know about models for transition?

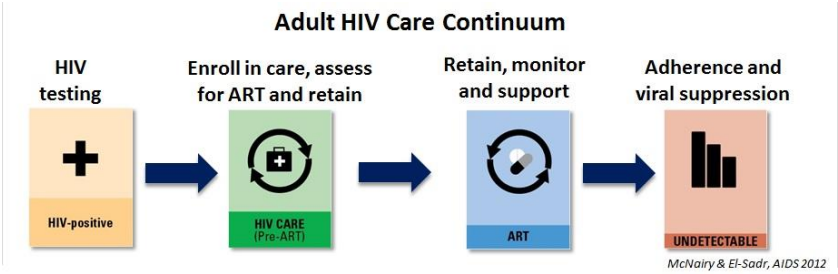
- No ‘tested’ models; several piloted; several described
  - Most programs introduce adolescents to adult care services through visits, joint clinics, or assisted referral
  - Toolkits, tools, supportive materials available, generic and program specific, common recommended program elements
- Transition between services must be
  - ***Tailored*** to the local situation
  - ***Individualized*** to the child, family and community context
  - ***Include*** core set of services addressing the specific needs of the population, particularly young women
- ***Ultimately the goal is successful engagement and retention in adult HIV services***

Essential services for adolescents living with HIV infection

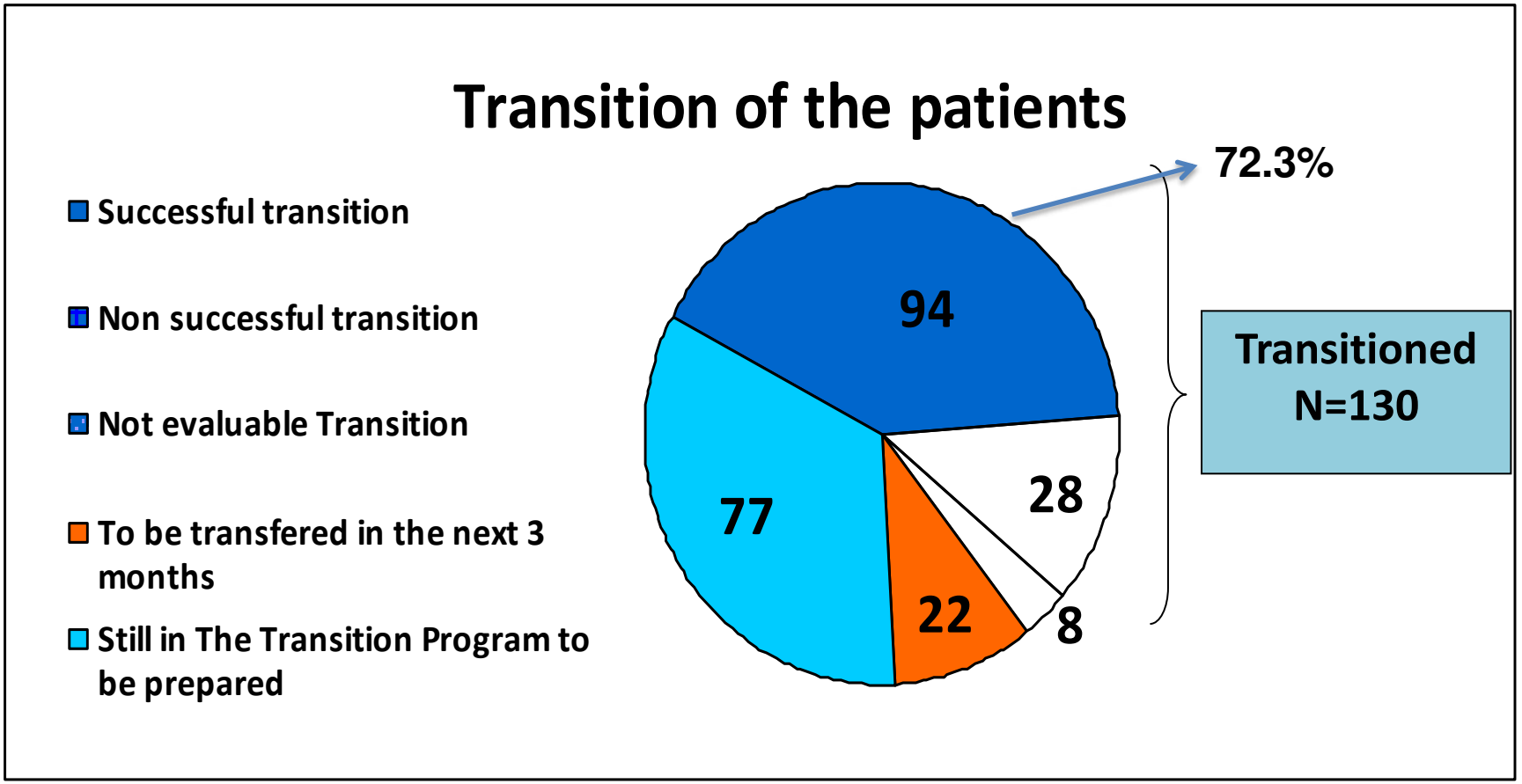
- Informed health care workers
- Advanced HIV management
  - Suitable ARV regimens,
  - Treatment of OI & complications
- Adherence support
- Sexual and reproductive health services (SRH)
  - Contraception & pregnancy care
- Prevention with positives
- Peer education and support services
- Mental health services
- Training in treatment and health literacy
- Community-based services
  - Access to housing, legal services
- Harm reduction
- Life skills training

What is successful transition and how do we measure it?

- Critically important to define outcomes
  - Retained in care?
  - Adherent to ART?
  - Uses contraception?
  - Uses condoms (secondary prevention)?
- Critically important to monitor individual outcomes post-transition
  - To support optimal health outcomes
  - Assess program strengths weaknesses



Transition outcomes HIV+ adolescents in Argentina



Caillaud, IAS 2014

Transition to adult care: mortality in perinatally-HIV+ youth in UK/Ireland

- Evaluated mortality 2006-2011 in UK/Ireland in 996 perinatally-infected youth ≥13 years, including 248 cared in 14 adult clinics.
- Median age at transfer 17 years (range 15-21) and at death 21 years(range 17-24)
- Estimated minimum mortality by age and type care in perinatally HIV-infected young people UK/Ireland:

Age Group/ Type Care	Number of deaths n=11	Mortality Rate/ 100 pt-yr	Rate Ratio
13-15 years, Pediatric	3	0.2 (0.1-0.6)	1.0
16-20 years, Pediatric	2	0.3 (0.1-1.0)	1.3 (0.2- 8.6)
16-20 years, Adult	4	0.5 (0.2-1.3)	2.7 (0.6-12.2)
≥21 years, Adult	4	0.9 (0.3-2.3)	4.9 (1.1-22.0)

Fish, HIV Med 2014

In Conclusion

- Large numbers of children with perinatal HIV infection are entering adolescence, a period of rapid and complex physical and emotional growth and development
- These youth are faced with a broad array of health and behavioral challenges as a consequence of complications of the disease as well as the treatments
- We are now challenged with both defining and meeting these health needs to ensure a safe and successful passage into adulthood
- Adult HIV programs will inherit this legacy and will be responsibility addressing the next many years of treatment that lie ahead for these young people

Acknowledgements

Thanks especially to Rohan Hazra, Claude Mellins, Lynne Mofenson, Zachary Peters, Annette Sohn, PHACS collaboration, CASAH collaboration