HIV in Adolescents

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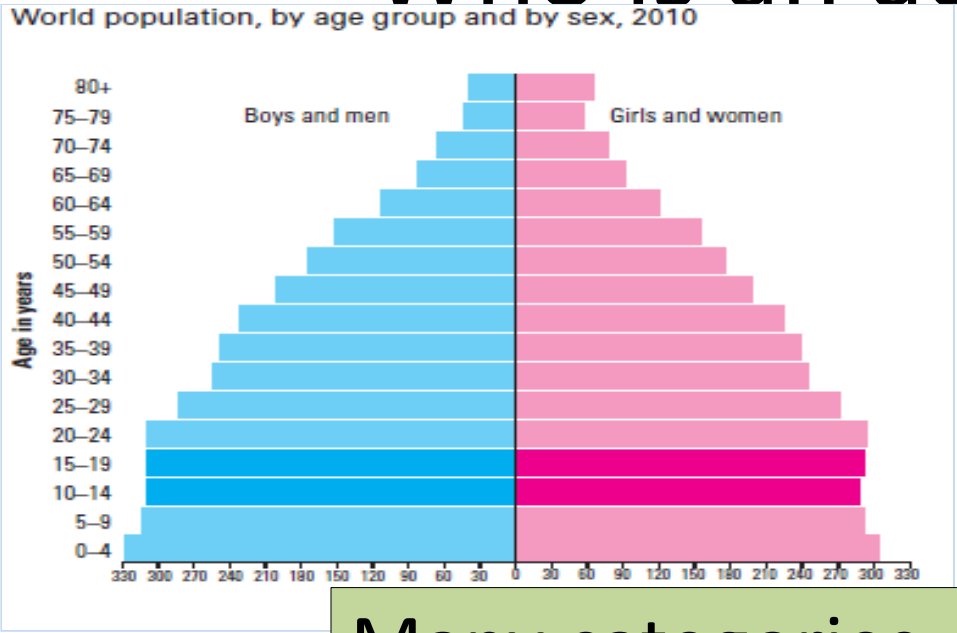
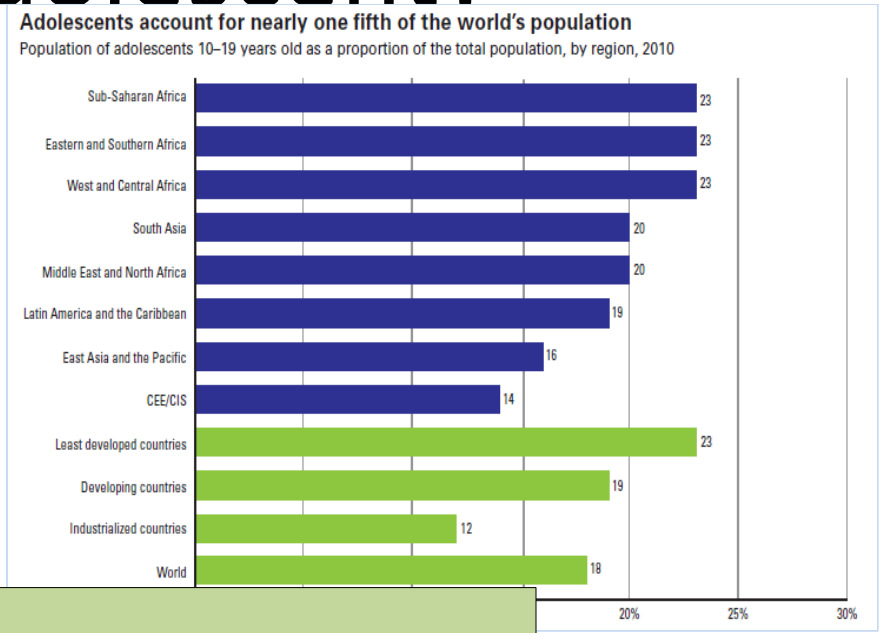
Overview

- Defining adolescence and specific issues
- Epidemiology
- ART - Specific considerations
  - Outcomes
- Adherence
- Risk taking behaviour
- Transition to adult care

Who is an adolescent?





Many categories:

- Married/unmarried
- School-going/out of school/working
- Sexually exploited
- Parents/orphans

Why are adolescents different?

- Transition period from childhood to adulthood characterized by physical, psychological, social and emotional maturation
- Changing body
- Changing mind
- Not happening together
- Sexual awakening
- Risk-taking, impetuous
- Autonomy
- Peer influence
- ‘Hot cognition’

A complex set of issues in HIV+

- Specific issues in
- Developmental outc
- May impact on behav
- Secondary transmission

Epidemiology

Adolescent HIV may fall into diverse categories:

- Resource-rich vs. resource-poor
- Perinatally/vertically infected HIV+ (PHIV+) vs. non-perinatally/behaviourally/horizontally infected HIV+ (BHIV+)
- Differing presentations
- Management issues may differ depending on when the adolescent presents and in which context BUT often overlap

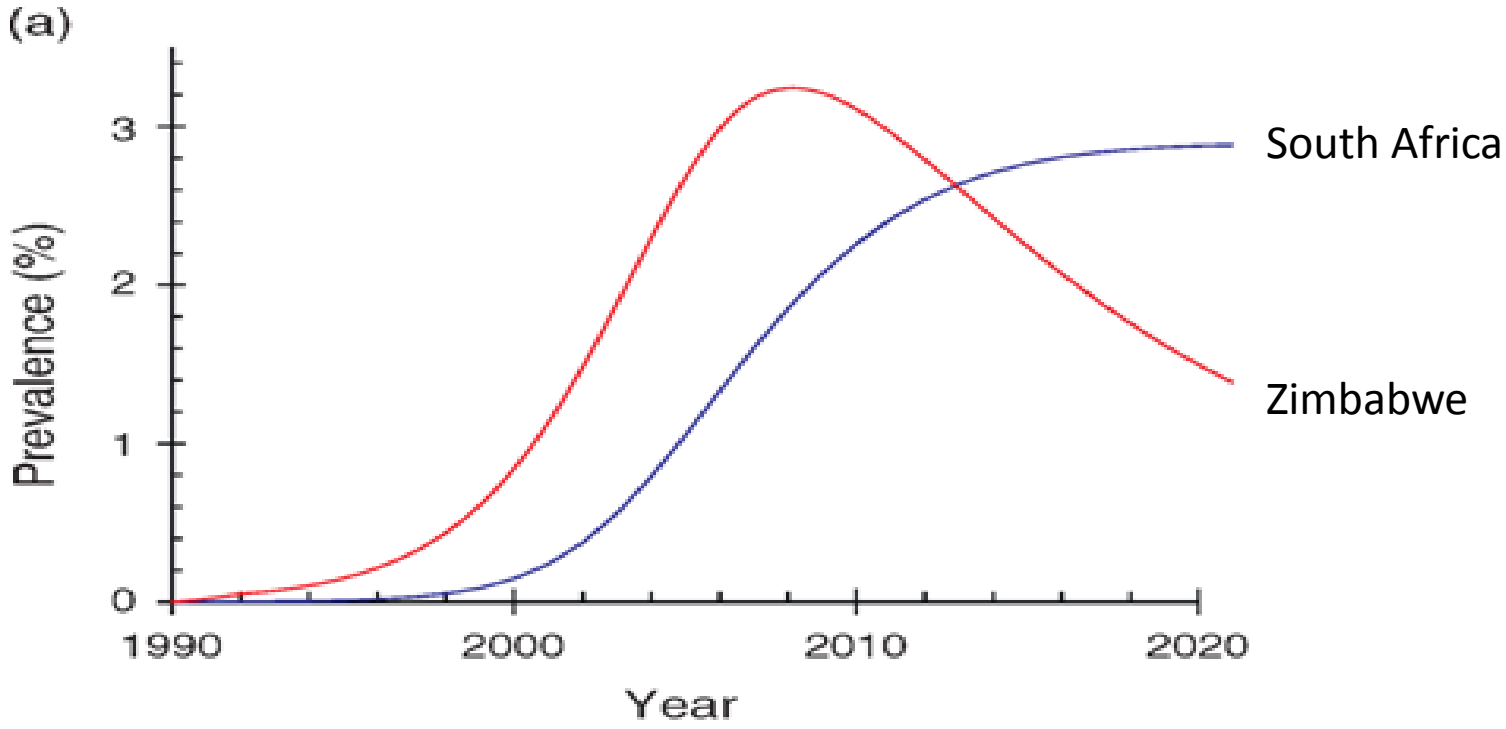
PHIV+ resource-rich settings

- Well controlled paediatric HIV infection since the mid-90s
- Current paediatric population is ageing or has already aged into adolescence with minimal new perinatal infection
- Adolescents are often treatment-experienced and may have multidrug ART resistance (previous exposure to mono/dual therapy or multiple regimens)

PHIV+ resource-limited settings

- May have a similar population to resource rich settings with ageing paediatric population on ART treatment
- Those on ART: generally less complicated prior treatment
- BUT frequently late presenters who are often extremely immunocompromised clinically and immunologically
- May test through research, clinic visits or during hospital admissions

PHIV+ resource-limited settings



Projected prevalence of vertically transmitted HIV in 10 year olds in SA and Zimbabwe. (Ferrand, AIDS 2009)

Estimated that 36% of HIV-infected infants are slow progressors with median survival of 16 years

Ferrand, *AIDS* 2009

Non-perinatally HIV +

- May present at various stages: possibly as a result of HCT campaigns/testing in research environments/PMTCT/ clinic visits or hospital admissions
- Sometimes may be difficult to distinguish PHIV+/Non-PHIV+ but this group usually predominantly female, history of sexual activity or intravenous drug use etc., may be HSV 2 +
- May have different needs but ART treatment the same

Ferrand R et al. *PLoS Medicine.* 2010

Access to ARVs in Botswana

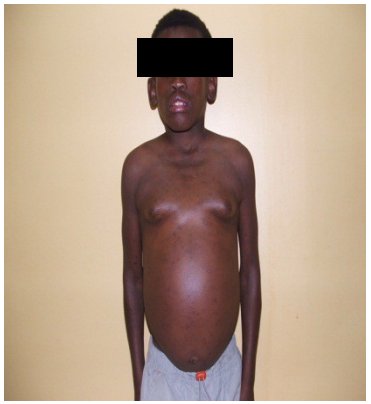
Antiretroviral treatment

- Adolescents have previously fallen into either paediatric or adult guidelines
- Move with youth-friendly focus to address group separately within guidelines documents
- Specific dosage and toxicity concerns related to age, weight and Tanner staging
- The simplest regimen possible should be chosen (not always possible with 2nd/3rd line)

Picture courtesy of WHO and Eric Miller

Specific issues with regimens

- Many FDCs for over 40 kg (Efavirenz dose)
- Side effects of drugs e.g. nausea/vomiting with aluvia
- **Toxicities:**
    - Tenofovir-related:
        - Renal tubular toxicity
        - Bone mineral density reduction
    - Fat redistribution syndrome
    - Anaemia with zidovudine (malaria areas)
    - Hyperlipidemia and metabolic syndrome
    - ABC HSR
    - EFV-related psychosis



Potential drug interactions

- Rifampicin-based TB therapy + nevirapine
- Rifampicin-based TB therapy and LPV/r (double LPV/r dose to 600 mg/m2)
- Antiepileptic agents and ART – sodium valproate preferred agent
- Hormonal contraceptives particularly COCs and POPs and ritonavir/ritonavir-boosted PI use not recommended

Outcomes on ART

- Some adolescents will have excellent outcomes
- BUT adolescence is a period of higher risk for poor adherence
- Southern Africa: Adolescents 50% lower adherence compared to adults and 70-75% lower chance of virological suppression at 1 and 2 years
- Lower CD4 recovery and shorter time to virological rebound if suppressed
- USA REACH cohort (BHIV+)
  - 41% of adolescents had >95% adherence
  - 37% of 120 adolescents ART after 3 years
    - 24% reached and maintained undetectable viral load, poor adherence main predictor of failure
  - Mean CD4 not statistically different to HIV-
- Comparative cohort USA: no difference in virological suppression between BHIV+ and PHIV+

Flynn et al *JAIDS* 2007; Nachega et al *JAIDS* 2010; Chandwani et al. *J Adolesc health* 2012

Adherence

- Poor adherence in adolescents not restricted to HIV
- Adherence is the single most challenging aspect of successful HIV care
- Non-adherence may be caused by any combination of structural, patient-related, provider-related, medication-related, disease related and psychologically-related factors
- Adherence is not stagnant and requires continuous reassessment

Factors associated with non-adherence

- Many factors are simple and practical
- Forgetting
- “Reminds me of HIV”
- Wanting a break from ART
- Complications in day-to-day routines
- Pill burden (“too many pills”)
- AIDS diagnosis/Advanced HIV disease
- Advanced age > 15 years
- Depression and PTSD
- Poor self image (stunting)
- Alcohol/substance abuse
- Dropping out of school
- Adverse effects of ART
- Structural barriers such as poverty and stigma
- Poor social support – orphans

MacDonnell *AIDS Behav* 2013; Rudy *AIDS PAT CARE & STDs* 2010; Mills *PLoS Med* 2006

Mechanisms to improve adherence

Medication-related barriers
Reduced pill burden (OD dosing, FDC)
Palatable formulations
Management of side effects
Anti-nausea, anti-diarrhoeal agents
Change timing of dosing
Regimen change

Patient-related factors
Disclosure
Bereavement and trauma counselling
Treatment of concurrent mental illness
Intensive HIV and ART education

Behavioural interventions
Motivational interviewing
Counselling, support groups
Life skills education
Parental/caregiver involvement
Buddy systems
Adherence clubs
Peer motivators/educators
Activity triggers (e.g. meals)
Calendars
Technological interventions
Pill boxes
Directly observed therapy
Anti-stigma campaigns

Structural Barriers
Address barriers such as transportation, child care, clinic hours
Education of clinic staff
Address stigma and discrimination

Resistance

- NNRTIs (NVP and EFV) and lamivudine low genetic barrier to resistance
- Continued failure on this regimen → accumulation of resistance to NRTIs
- PI resistance is uncommon and sustained levels of viremia, with low level drug circulating for prolonged periods before increased resistance risk
- Need to address adherence issues before any switch to 2nd/3rd line regimens

PENPACT -1 *Lancet Infectious Disease* 2011

Potential solutions

- Need to try and get the non-adherent adolescent through with minimal damage!!
- Drug holidays (this may be the worst option immunologically)
- Holding regimens
  - 3TC monotherapy
  - Combination NRTIs
- New regimens (may require access to third line drugs)

Siberry *JAIDS* 2011; Abadi *JAIDS* 2006; Fairlie 2013 (unpublished)

Risk-taking behaviour

- PHIV+ mixed findings regarding risky sexual activity and substance abuse
- May delay sexual activity because of concerns regarding HIV, may also be developmentally and neurocognitively delayed
- PHIV+ lower rates of substance abuse and risky sexual behaviour than general adolescent population
- High levels of transactional sex amongst AIDS orphans
- Both groups: those who are sexually active frequently engage in unprotected sex (up to 65%)
- Low rates of disclosure to sexual partners (about a third)
- High risk sexual behaviour and substance abuse associated

Burungi H *AIDS CARE* 2009; Mellins C *AIDS PATIENT CARE and STDs* 2011;
Bauermeister J *Sex Res* 2012; Cluver *JAIDS* 2011; Elkington *J Adol Health* 2009;
Youth Risk Behaviour Surveillance 2012 *MMWR*.

Potential impact of risky sexual behaviour

- Recent study PHIV+
  - 28% reported sexual intercourse; median age of coitarche of 14 years; 62% reported unprotected sexual intercourse, and only 33% of youth disclosed their HIV status to their partners
  - For those not sexually active at baseline ART non-adherence was associated with sexual debut
  - Genotypic resistance in the 42% of sexually active youth with viral loads ≥5,000 copies/mL, identifying 62%, 57%, 38%, and 22% to NRTIs, NNRTIs, PIs, and all 3 ARV classes, respectively
  - Concern for secondary transmission (horizontal and vertical) multi-resistant HIV

Tassiopoulos *CID* 2013

The special needs of HIV-infected adolescents

- Simplification of ART as far as possible
- Addressing adherence and other risk-taking behaviour
- Assistance with disclosure both to and by the adolescent
- Support for sexual and reproductive health issues especially regarding contraceptive use and safer sex practices
- Support for mental health issues including unresolved grief, depression, anxiety, ADHD, PTSD and substance abuse
- Facilitation of psychometric testing where necessary to ensure appropriate education

Transition to adult care

- Some clinics may have no separate adolescent space so may require mental shift rather than physical
- Ultimate goal of successful adolescent HIV care
- High-risk period for non-adherence and loss to follow-up
- Many adolescents have complex psychosocial and ARV treatment histories (need good history taking and good communication)
- Ongoing need to support adherence, SRH needs, reduction of risky behaviours and identification and treatment of mental health problems

Case study XD

- 17 year old female
- She was first seen at the HIV clinic when she was 8 years old , mom had been recently diagnosed HIV+
- Clinically well at that time with WHO stage I disease
- CD4 count was 160 (13%); HIV viral load was 23 000 copies/ml and full blood count was normal
- Parents have both died (mother in 2009 and father in 2010)
- Her 3 younger siblings moved to grandmother.
- Presents as withdrawn and sad although she seems to be managing school and chores
- She reports that her grandmother frequently shouts at her for staying out late in the evenings especially when she is out with her much older 'male friend'
- He has attended clinic with her on the last 2 occasions and waits in the waiting room (today he appears intoxicated)

- XD was started on cART on the 6/07/2005 based on her CD4 count. She received D4T, 3TC and efavirenz as per local guidelines at the time
- She was virally suppressed from January 2006-July 2009, with an increasing CD4 count and percentage
- She remained clinically well and her weight is 58 kg, height 167 cm

Progress…..

Switched to 2nd line AZT/DDI/Aluvia

	July 2009	Oct 2009	Jan 2010	July 2010	Jan 2011	July 2011	Jan 2012	April 2012	Oct 2012	Feb 2013	June 2013
CD4 #	500	460	480	430	600	620	580	540	530		
CD4 %	23	22	23	21	24	24	25	21	22		
VL	12888	15300	10000	16566	11234	9034	7600	17000	18675	16543	15467

Discuss the management of this adolescent so far. Has it been appropriate?

- Started appropriately on ART
- Had a VL done 3 months after elevated VL in July 2009 and 3 months after that
- Recent bereavement of mother and illness of father had an impact on VL
- Delay in switching to 2nd line ART regimen as she had been failing for about a year by that stage with risk of accumulation of resistance
- Hopefully adherence issues were being addressed throughout this period
- This is a frequent scenario with adolescent patients, who have a much greater risk of poor adherence. Ongoing adherence counseling with an aim at identifying barriers to adherence is essential.
- Bereavement counseling would have been appropriate.
- If this was a primary centre, the patient should have been referred as failing 2nd line

Tabulate your approach to this adolescent in terms of medical, sexual and reproductive health and psychosocial concerns that need to be considered in this adolescent

Elevated VL on 2nd line

Needs screen for OI or any other potential contributors to the increased VL

Is stable so could consider holding regimen but needs close monitoring

Needs DRT to guide further choices regarding simplification of regimen or the need for third line.

DDI difficult to take, try and simplify the regimen.

Sexual activity? (voluntary or involuntary)

Needs contraceptive advice (should not take COC pill or POCP)

Education regarding condom use

STI screen

Screen for intimate partner violence

Adherence needs to be addressed thoroughly

Disclosure (when was she disclosed to if ever? Has she disclosed to her 'friend'?)

Mental health screen especially for anxiety, PTSD, depression,

Screen for alcohol use

Screen for other substance use

Possible unresolved grief issues

Conflict with caregiver

Assess caregiving responsibilities in the home

Ask about school performance and future education plans

Assess if family receiving social grants

How would you manage her HIV disease further?

- Consider holding regimen
- Need to aggressively address adherence
- Try and simplify regimen (base this on a resistance test but only do once adherence is good otherwise drug pressure will be absent and mutations may be missed).
- Where possible, reduce the pill burden (e.g. stop multivitamin tablet if not necessary. She should not be on CPT at this CD4).
- Third line regimen to be considered with resistance testing results
- Ensure that there is safety both in the home and with her 'friend'/partner
- Refer if there are any mental health or substance abuse problems
- If appropriate refer to social worker for access to social grant
- If she has not been disclosed to, complete the disclosure process

If she fell pregnant would your management plan change?

- Do not consider holding regimen as need full VL suppression to protect fetus from infection
- Unable to take FDC as most likely resistant to EFV and 3TC/FTC
- Urgently needs DRT to asses for 3rd line
- Inform her of her right to TOP and facilitate access if she opts for abortion
- If there is rape refer for appropriate counseling and legal support
- Educate on safety in intimate partner relationships, fertility control and sexual coercion if necessary
- Discuss PMTCT alternatives

Conclusion

- With PMTCT success adolescents will form the bulk of PHIV+ population
- HIV+ adolescents may do well on ART BUT it is a high-risk period for non-adherence
- HCW attitude is key!!!
- Need to support specific needs of adolescents while encouraging as safe as possible behaviour (adherence, sexual and substance abuse risks)
- Transition to adult care requires planning and thorough referral to avoid loss to follow-up and virological failure

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