Adolescents-problem areas

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HIV Symposium

9 May 2015

SS

- 17 year old female
- First presentation to care 31/1/2005 (8 years)
- Perinatally HIV-infected
- WHO stage 1; Immunologically stage 3 CD4 198 (11.9%)
- Started D4T/3TC/EFV on 27/5/2005
- Did well initially: remained virally suppressed
- Bloods 8/2/08: VL < 25 copies/ml and CD4 562 (27.4%)

Continued….

Ongoing adherence concerns:

- Living with aunt, mom looking after her ill mother
- Little in way of treatment support
- Only disclosed to when 12y6m

Date	Jul 08	Aug 08	Dec 08	Mar 09	Oct 09	Feb 10	May 10	Oct 10	Feb 11
Age	12y4m	12y5m	12y7m	12y11	13y6	13y10	14y1	14y7	14y10
CD4 #	261			198		247	205	221	224
CD4%	14			14.6		14.5	12.9	12.47	17.72
VL	15000	150	37000	18000	25	1800	1200	46888	1577

DRT on 25/08/2008: No resistance detected

Changed to second line 16/3/2011 (ABC/TDF/Aluvia)

True/false

1. As SS had no resistance she should not have switched regimens
2. AZT/3TC & LPV/r would have been a superior choice of 2nd line
3. Adolescents of 12 years and younger can use TDF without any concern
4. TDF can safely be used in pregnant adolescents > 12 years and > 40 kg

On second line….

- Well clinically

Date	Oct 11	April 12	June 12	Sep 12	Nov 12	May 12
CD4#		167	214		228	130
CD4%		11.9	15.8			11.2
VL	188	4130	11958	154122	1347	124293

Vomiting and unable to swallow alluvia 200/50, switched to 100/25mg
Ongoing poor adherence and missed appointments

Seen in July 2013

- LMP April 2013
- Pregnant, does not want to explore option of TOP
- O/E HOF about 16 weeks
- Has not taken ART since realized she was pregnant
- Advised by her sister that ART may be harmful to the baby……

Further progress….

Booked ANC

Male infant born
Birth PCR negative
Received kal/AZT/3TC

3m: Baby admitted:
kwashiorkor, GE,
LRTI(diluting formula)
PCR negative

	13 Oct 2013	21 Nov 2013	23 Dec 2013	15 Jan 2014	18 Mar 2014	17 Apr 2014
VL	59894	137025		135174		
CD4 (%)	106 (9.9%)			163 (11.7%)		

Changed to combivir and aluvia

DRT: No resistance detected

Has defaulted visits again since May

Options for contraception in SS are: (choose as many as applicable)

1. CU-IUD
2. COC or progesterone only pill
3. DMP
4. Implanon
5. Condoms

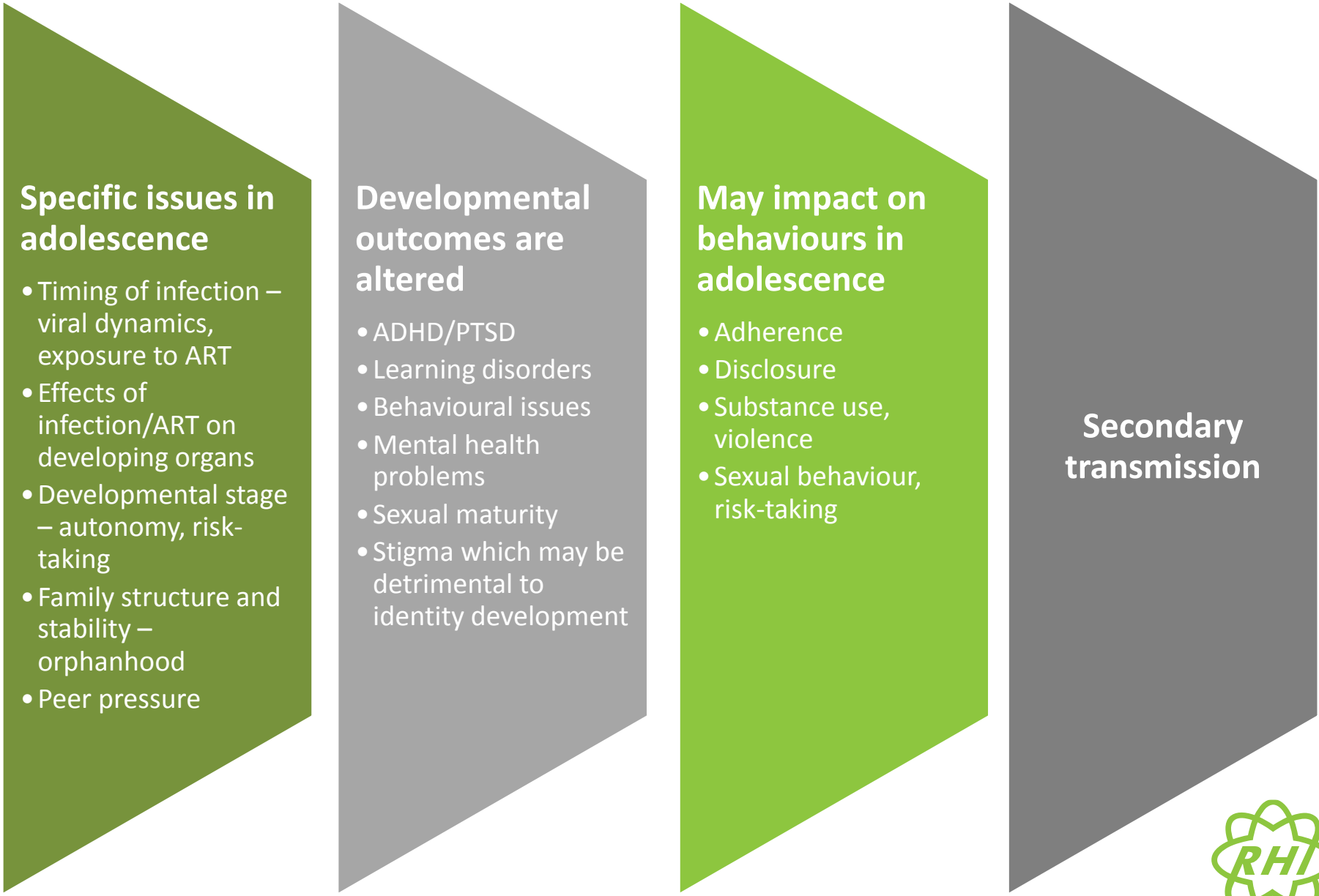
Issues.....

- Teenage pregnancy
- High transmission risk with high VL and low CD4
- ? Resistant virus most likely
- Difficulties with managing these HIV-exposed infants (Maternal VF)
- Failed opportunities for FP
- Disclosure

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+



Approaching adolescents…

- Dress down ☺
- Always talk about sex
- Always talk about alcohol/drugs (rock n roll optional!)
- Have no expectations….
- But expect to be surprised
- Give whatever support you can…..you may be this young person's ONLY role model

Adherence

- Adolescence is increased risk period for poor 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 high levels of viremia for prolonged periods before increased resistance
- Need to address adherence issues before any switch to $2^{nd}/3^{rd}$ line regimens

PENPACT -1 *Lancet Infectious Disease* 2011

Potential solutions

- Need to try and get the non-adherent child and 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)

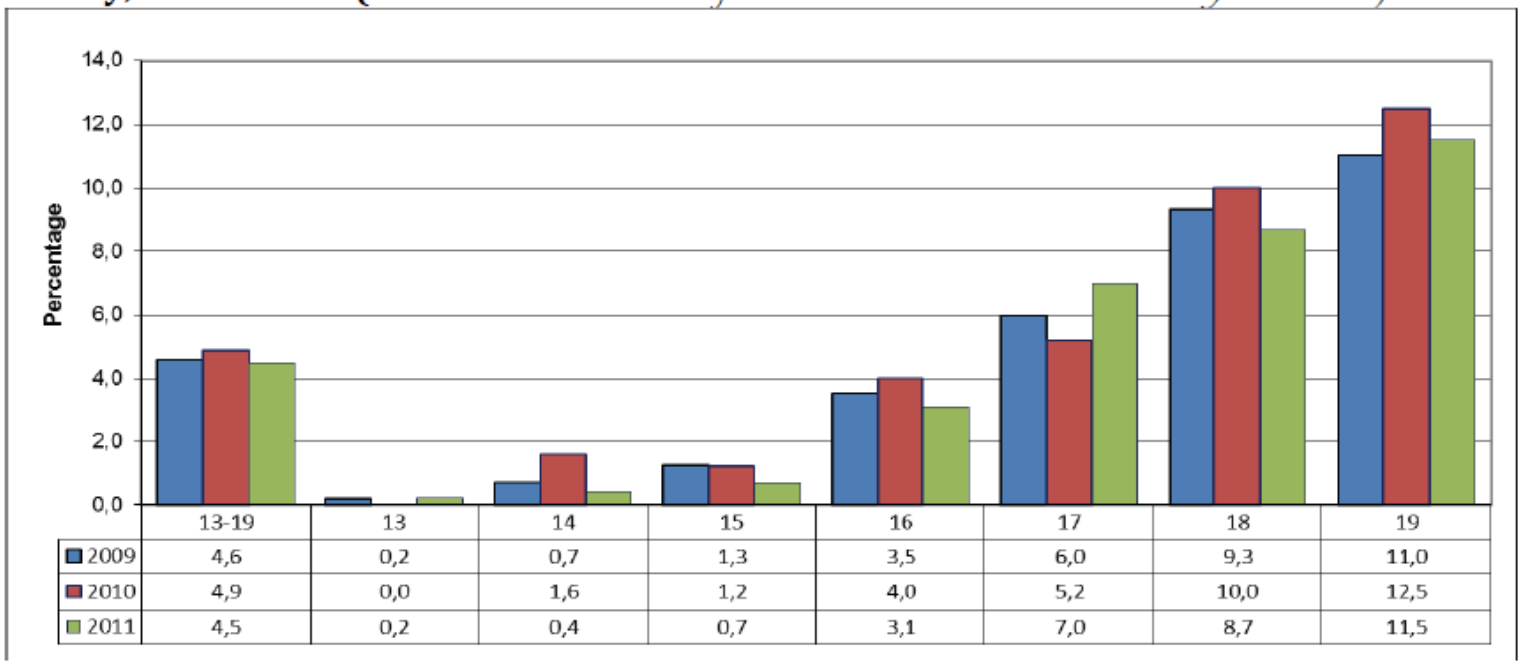
Risk-taking behaviour

- 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*.

Pregnancy and SA adolescents

Table 1: Percentage of females aged 13–19 who were pregnant during the year preceding the survey, 2009–2011 (*source: Stats South African General Household Survey 2012:18*)



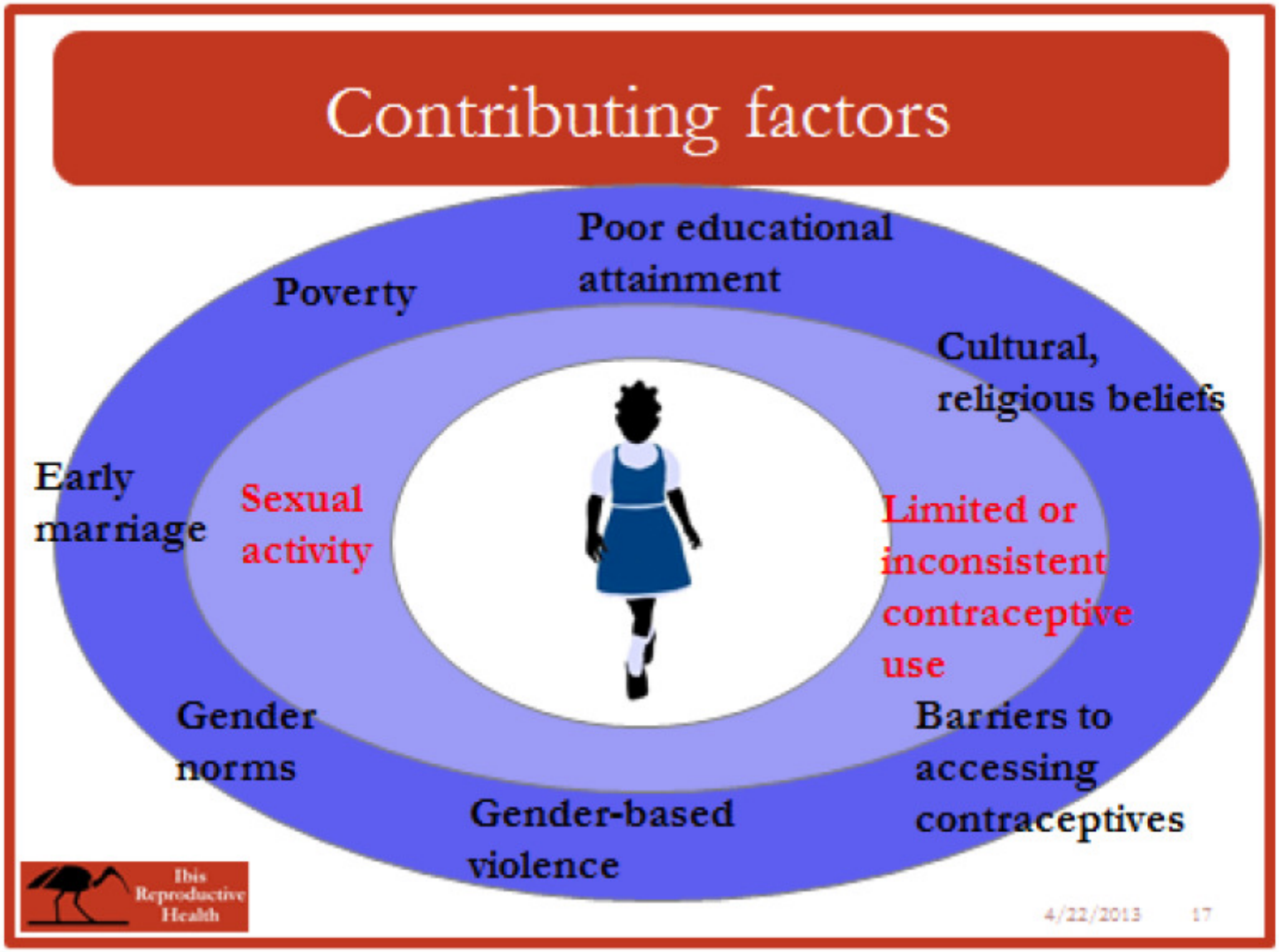
	13-19	13	14	15	16	17	18	19
2009	4,6	0,2	0,7	1,3	3,5	6,0	9,3	11,0
2010	4,9	0,0	1,6	1,2	4,0	5,2	10,0	12,5
2011	4,5	0,2	0,4	0,7	3,1	7,0	8,7	11,5

Pregnancy rates in adolescent women

- Up to 30 % of adolescents in SA report ever having been pregnant
- QA Karim et al: Open cohort recruited from FP and STI clinic for longitudinal HIV risk reduction study 2004-2007; KZN
- 27% of women under 18 years HIV+
- Of HIV-
    - Pregnancy rates 23.7 (>18) and 16.4/ 100wy (<18)

QA Karim; *AIDS Behaviour* 2012

Factors Contributing to teenage pregnancy



Source: Flanagan et al, 2013, Teen pregnancy in South Africa: A literature review examining contributing factors and unique interventions

The law and adolescent sex

Sexual offences act:

- Section 15: criminalises acts of sexual penetration by adults with children between the ages of 12 and 16 years, despite their consent
- Section 16 criminalises sexual penetration between consenting young people between the ages of 12–16 years
- Court case 2013: *Teddy bear clinic and partners vs Minister of Justice*: "Constitutional Court found that sections 15 and 16 of the Act are unconstitutional in that they infringe the rights of adolescents (12- to 16-year olds) to dignity and privacy, and further in that they violate the best-interests principle"

Children's Act 2010

CRIMINAL LAW (SEXUAL OFFENCES AND RELATED MATTERS) AMENDMENT ACT 32 OF 2007

* **eliminating the differentiation drawn between the age of consent for different consensual sexual acts and providing for special provisions relating to the prosecution and adjudication of consensual sexual acts between children older than 12 years but younger than 16 years;**

1 In *Teddy Bear Clinic for Abused Children and Another v Minister of Justice and Constitutional Development and Another* 2014 (2) SA 168 (CC), ss. 15 and 16 were found to be inconsistent with the Constitution and invalid to the extent that they impose criminal liability on children under the age of 16 years. The declaration of invalidity was suspended for a period of 18 months in order to allow Parliament to correct the defects. A moratorium was placed on all investigations into, arrests of, prosecutions of, and criminal and ancillary proceedings against, children under the age of 16 years in relation to these provisions, pending Parliament's correction of the defects. Furthermore, children under the age of 16 years who have been convicted of an offence referred to in s. 15 or 16, or issued a diversion order following a charge under those provisions, are not to appear in the National Register of Sex Offenders, and are to be issued certificates of expungement.

2 In *Teddy Bear Clinic for Abused Children and Another v Minister of Justice and Constitutional Development and Another* 2014 (2) SA 168 (CC), ss. 15 and 16 were found to be inconsistent with the Constitution and invalid to the extent that they impose criminal liability on children under the age of 16 years. The declaration of invalidity was suspended for a period of 18 months in order to allow Parliament to correct the defects. A moratorium was placed on all investigations into, arrests of, prosecutions of, and criminal and ancillary proceedings against, children under the age of 16 years in relation to these provisions, pending Parliament's correction of the defects. Furthermore, children under the age of 16 years who have been convicted of an offence referred to in s. 15 or 16, or issued a diversion order following a charge under those provisions, are not to appear in the National Register of Sex Offenders, and are to be issued certificates of expungement.

The law and contraception

- Adolescents 12 years by law should receive condoms at their request
- Other contraception:
  - at least 12 years of age and
  - proper medical advice is given
  - medical history is taken
  - appropriate examinations
  - ? Medical exclusions
- Right to confidentiality unless concern about physical or sexual abuse, or deliberate neglect

Children's Act 2010

The law and HCT

- Able to consent to HIV testing if:
- > 12 years old
- < 12 years old and able to demonstrate sufficient maturity to understand benefit, risks and social implications
- Maturity assessment *(difficult!!!)*
  - Age
  - Knowledge
  - Views
  - Personal circumstances

Children's Act 2010

Contraception use

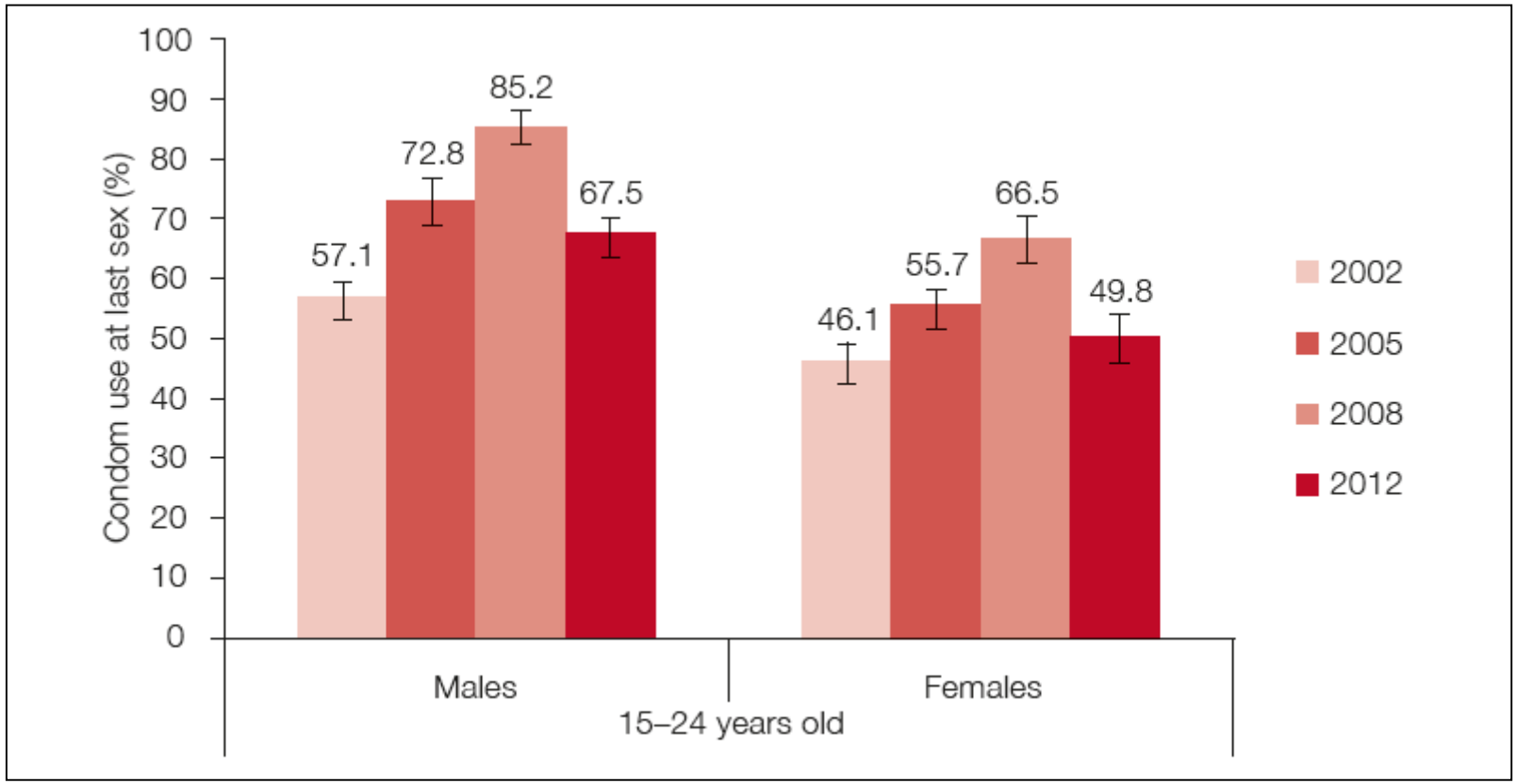
- Gaps in the literature regarding pregnancy intentions and contraception
- US-based review article
  - 51 % PHIV+ adolescents use condoms
  - Injectables alone 21%
  - Condoms & injectables/oral 16%
  - Overall HIV+ more likely to consistently use contraception compared to HIV- (56% vs. 44%)
  - 83% pregnancies unintended

QA Karim et al:

- Contraception use 43.8% (6m); 51.6% (12m)
- Any STI symptoms 11.4% (6m); 9.7% (12m)

Carter et al. *AIDS PATIENT CARE and STDs. 2013*

Condom use at last sex by age, sex



58.3% 15-24 year olds using condoms, highest percentage age-wise

HSRC Report 2012

What are the barriers to accessing contraception?

- HEALTH CARE WORKER ATTITUDES
- Side effects especially weight gain and mood changes
- Fears of using IUD
- Drug-drug-interactions
- Stopping/irregular periods
- Misinformation or poor education regarding contraception
- Not integrated into HIV care (hospital-based clinics)

Contraceptive options in young women

- WHO:

MEC categories for contraceptive eligibility	
1	A condition for which there is no restriction for the use of the contraceptive method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4	A condition which represents an unacceptable health risk if the contraceptive method is used.

MEC= Medical Eligibility Criteria for Contraception

WHO 2014

Summary of recommendations for adolescent contraception

Recommended contraceptive methods for young people:

- Abstinence
- Delay sexual debut
- Barrier method (strong reinforcement of condom use) with highly effective contraception:
  - combined hormonal contraception
  - progestogen-only injection
  - Cu IUD
  - LNG-IUS
  - progestogen-only implant
- Emergency contraception to be promoted and accessible in the event of unprotected intercourse, method misuse or failure

DoH Contraception Guidelines;
Adolescent Toolkit Wits RHI 2014

Summary of options for contraception for adolescents living with HIV

Method	Common side effects	Common contraindications *(not all-inclusive)*	Drug interactions: TB Rx	Drug interactions: ART	Prevention		Comment/recommendation
					STI	HIV	
Male condom	None	None	None	None	✓	✓	Promote condom use for all adolescents. Consistency, correct use and with confidence
Female Condom	None	None	None	None	✓	✓	Promote condom use for all adolescents. Consistency, correct use and with confidence
COCs	Nausea, inter-menstrual bleeding, mild headaches, breast tenderness	History of thrombosis, hypertension	**Rifampicin** - do not use together (WHO MEC 3)	**RTV-boosted PIs** – do not use together (WHO MEC 3) **NNRTIs** – generally can use, add condom (WHO MEC 2)	x	x	Client-dependent contraception: adherence essential. Can be used where adherence ensured. Combine with condom use
Injectable (DMPA/NET-EN)	Changes in menstruation (irregular, prolonged, heavy, amenorrhoea) and weight gain	Undiagnosed vaginal bleeding	**DMPA:** none. (WHO MEC 1) **NET-EN:** mild interaction with rifampicin. To add condom (WHO MEC 2)	**DMPA:** none. WHO MEC 1) **NET-EN:** mild interaction with PIs and NNRTIs. To add condom (WHO MEC 2)	x	x	Recent studies have shown that DMPA may increase HIV transmission risk (until further research has been conducted, WHO stance: condom use is strongly recommended (WHO MEC 1). Client-independent contraception
Cu IUD	Menstrual changes (bleeding may be heavier, longer and more cramps)	Current AIDS and unwell, current cervicitis/PID	None	None	x	x	Reliable, long acting reversible contraceptive method. Client-independent method. May be used as emergency contraception. Combine with condom use. Can be inserted if client is well (WHO MEC 2). *Note: Unwell HIV positive – WHO MEC 3.*
LNG IUD	Irregular and infrequent bleeding initially with development of amenorrhoea later	Current AIDS and unwell, current cervicitis/PID	None	None	x	x	Not currently available in the PHC setting. Reliable, long acting reversible contraceptive method. client-independent method. Cannot be used for emergency contraception. Combine with condom use. Can be inserted if well (WHO MEC 2). *Note: Unwell HIV positive - WHO MEC 3*
Progestogen-only implants	Irregular bleeding and amenorrhoea, but less pronounced than with injectables	Undiagnosed vaginal bleeding	Mild interaction with rifampicin. Avoid concurrent use. (See comment)	Mild interaction with PIs and NNRTIs. Avoid concurrent use. (See comment)	x	x	**Note:** recent evidence has shown that EFV, rifampicin and certain anticonvulsants should not be used with the implants due to reduced contraceptive efficacy. If already inserted, it may be removed and an alternative method used, or an additional non-hormonal method should be added (such as IUD or condom use).
Emergency contraceptive pills	Nausea, vomiting, headaches, fatigue, cycle irregularities	Incident occurred more than 120hrs ago	With Rifampicin. No dose adjustment recommended	With PIs. No dose adjustment recommended	x	x	All clients should be aware of the availability of this method. Consider emergency IUCD use where pill use is inappropriate

Quick Reference Chart for the WHO Medical Eligibility Criteria for Contraceptive Use –

to initiate or continue use of combined oral contraceptives (COCs), depot-medroxyprogesterone acetate (DMPA), progestin-only implants, copper intrauterine device (Cu-IUD)

CONDITION		COC	DMPA	Implants	Cu-IUD
Pregnancy		NA	NA	NA	
Breastfeeding	Less than 6 weeks postpartum				NC
	6 weeks to < 6 months postpartum				
	6 months postpartum or more				
Postpartum (non-breastfeeding) VTE = venous thromboembolism	< 21 days				NC
	< 21 days with other risk factors for VTE*				
	≥ 21 to 42 days with other risk factors for VTE*				
	< 48 hours including immediate post-placental	NC	NC	NC	
	≥ 48 hours to less than 4 weeks				
	Puerperal sepsis				
Postabortion	Immediate post-septic				
Smoking	Age ≥ 35 years, < 15 cigarettes/day				
	Age ≥ 35 years, ≥ 15 cigarettes/day				
Multiple risk factors for cardiovascular disease					
Hypertension BP = blood pressure	History of (where BP cannot be evaluated)				
	BP is controlled and can be evaluated				
	Elevated BP (systolic 140 - 159 or diastolic 90 - 99)				
	Elevated BP (systolic ≥ 160 or diastolic ≥ 100)				
	Vascular disease				
Deep venous thrombosis (DVT) and pulmonary embolism (PE)	History of DVT/PE				
	Acute DVT/PE				
	DVT/PE, established on anticoagulant therapy				
	Major surgery with prolonged immobilization				
Known thrombogenic mutations					
Ischemic heart disease (current or history of) **or stroke** (history of)				I C	
Known hyperlipidemias					
Complicated valvular heart disease					
Systemic lupus erythematosus	Positive or unknown antiphospholipid antibodies				
	Severe thrombocytopenia		I C		I C
	Immunosuppressive treatment				I C
Headaches	Non-migrainous (mild or severe)0	I C			
	Migraine without aura (age < 35 years)	I C			
	Migraine without aura (age ≥ 35 years)	I C			
	Migraines with aura (at any age)		I C	I C	
Unexplained vaginal bleeding (prior to evaluation)					I C

CONDITION		COC	DMPA	Implants	Cu-IUD
Gestational trophoblastic disease	Regressing or undetectable β-hCG levels				
	Persistently elevated β-hCG levels or malignant disease				
Cancers	Cervical (awaiting treatment)				I C
	Endometrial				I C
	Ovarian				I C
Breast disease	Undiagnosed mass	**	**	**	
	Current cancer				
	Past w/ no evidence of current disease for 5 yrs				
Uterine distortion due to fibroids or anatomical abnormalities					
STIs/PID	Current purulent cervicitis, chlamydia, gonorrhea				I C
	Vaginitis				
	Current pelvic inflammatory disease (PID)				I C
	Other STIs (excluding HIV/hepatitis)				
	Increased risk of STIs				
	Very high individual risk of exposure to STIs				I C
Pelvic tuberculosis					I C
Diabetes	Nephropathy/retinopathy/neuropathy				
	Diabetes for > 20 years				
Symptomatic gall bladder disease (current or medically treated)					
Cholestasis (history of)	Related to pregnancy				
	Related to oral contraceptives				
Hepatitis	Acute or flare	I C			
	Chronic or client is a carrier				
Cirrhosis	Mild				
	Severe				
Liver tumors (hepatocellular adenoma and malignant hepatoma)					
HIV	High risk of HIV or HIV-infected				
AIDS	No antiretroviral therapy (ARV)				I C
	Clinically well on ARV therapy	see drug interactions			
	Not clinically well on ARV therapy	see drug interactions			I C
Drug interactions, including use of:	Nucleoside reverse transcriptase inhibitors				
	Non-nucleoside reverse transcriptase inhibitors				
	Ritonavir, ritonavir-boosted protease inhibitors				
	Rifampicin or rifabutin				
	Anticonvulsant therapy***				

Source: Adapted from **Medical Eligibility Criteria for Contraceptive Use, 4th Edition**. Geneva: World Health Organization; 2010.
Available: http://www.who.int/reproductivehealth/publications/family_planning/en/index.html

Category 1 There are no restrictions for use.

Category 2 Generally use; some follow-up may be needed.

Category 3 Usually not recommended; clinical judgment and continuing access to clinical services are required for use.

Category 4 The method should not be used.

Unlike previous versions of the MEC Quick Reference Chart, this version includes a complete list of all conditions classified as Category 3 and 4 by WHO.

I/C Initiation/Continuation: A woman may fall into either one category or another, depending on whether she is initiating or continuing to use a method. Where I/C is not marked, the category is the same for initiation and continuation.

NA Not Applicable: Women who are pregnant do not require contraception.

NC Not Classified: The condition is not part of the WHO classification for this method.

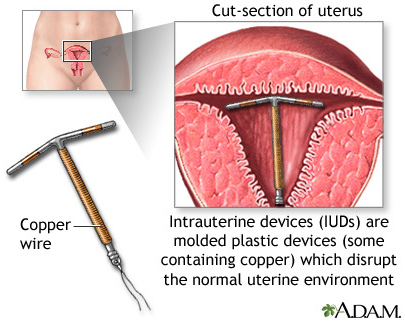
* Other risk factors for VTE include: previous VTE, thrombophilia, immobility, transfusion at delivery, BMI > 30 kg/m2, postpartum hemorrhage, immediately post-caesarean delivery, pre-eclampsia, and smoking.

** Evaluation of an undiagnosed mass should be pursued as soon as possible.

*** Anticonvulsants include: phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine, and lamotrigine. Lamotrigine is a category 1 for implants.

Emergency contraception

- Need to inform adolescents that this is an option for them
- CU IUD: Inserted within five days of unprotected intercourse, most effective form of emergency contraception available
- Emergency contraceptive pill: one dose of levonorgestrel 1.5 mg, taken within five days (120 hours) of unprotected intercourse
- Opportunity for intervention: unprotected intercourse/misuse or failure contraception or sexual assault



Specific points…..

- Concern regarding EFV and Implanon-> may be up to 12 % reduction in efficacy
- PI and COC
- With CU IUD, increased bleeding, may be increased risk factor for transmission of HIV
- DMPA may increase risk of HIV acquisition
- WHO:

"Given the importance of this issue, women at high risk of HIV infection should be informed that progesterone-only injectables may or may not increase their risk of acquisition."

WHO 2014 updates

Adolescents and PMTCT

- Horwood et al:
  - HIV prevalence, health care usage (ANC&PNC) women age 12-39 attending 6 EPI clinics in KZN
  - Adolescent women compared to over 20 years
  - Higher numbers adult women reported being HIV+; having a CD4 count done; receiving the result and access to PMTCT
  - Higher transmission rate in adolescent mothers: 10.8% vs 6.1%
  - Worrying: this despite adolescent mothers being as likely as adults to attend 4 clinic visits

= SYSTEM FAILING YOUNG HIV+ MOTHERS AND THEIR CHILDREN

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

STI management

- Syndromic approach: WHO/local guidelines
- Opportunity for education regarding STI and prevention (including HIV)
- Opportunity for HIV testing
- Opportunity to offer contraception and re-enforce condom use
- Offer treatment of current sexual partner
- Need to handle sensitively

STI: Syndromic Approach

Males

- Male urethritis syndrome
- Genital ulcer syndrome
- Scrotal swelling/pain
- Balanitis/balanoposthitis (BAL)
- Bubo
- Genital warts
- Pubic lice

Females

- Vaginal discharge syndrome
- Candidiasis/bacterial vaginosis
- Lower abdominal pain
- Genital Ulcer Syndrome
- Bubo
- Genital warts
- Pubic lice

Pre-and post exposure prophylaxis

- PrEP studies have not included adolescents because of issues around consent

PEP:

- Offer post a sexual assault
- Offer to the partner of a discordant couple if burst condom or unprotected sex
- Follow PEP guidelines

Conclusions

- Adolescents are sexually active and need full access to SRH services
- This requires youth friendly services and the correct attitude from HCW
- Many contraceptive options available
- Recognise and treat STIs
- Beware the contradictions in the law!

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

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