HIV, Fertility and Contraception in the era of U=U

NHIVNA 2018

Yvonne Gilleece
Consultant in HIV and Sexual Health
Brighton &Sussex University Hospitals NHS Trust
Honorary Senior Lecturer Brighton & Sussex Medical School

brighton and sussex medical school

The Lawson Unit
LEADING HIV CARE FOR BRIGHTON

Brighton and Sussex University Hospitals NHS Trust

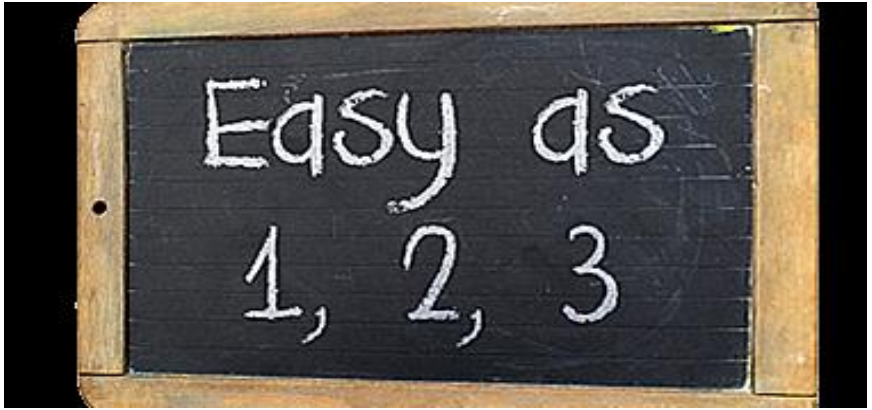
Disclosures

- I have received Honoria for educational meetings and advisory boards from ViiV, Janssen and Gilead

Introduction

1. HIV in the era of cART
2. Fertility
3. Conception and pregnancy

HIV, Fertility and Contraception in the era of U=U



1. Prescribe/take your ARVs
2. Use contraception to avoid pregnancy
3. If you/your partner want to get pregnant have unprotected sex

Thank you!

brighton and sussex medical school

The Lawson Unit
LEADING HIV CARE FOR BRIGHTON

Brighton and Sussex University Hospitals NHS Trust

Thank you!

brighton and sussex medical school

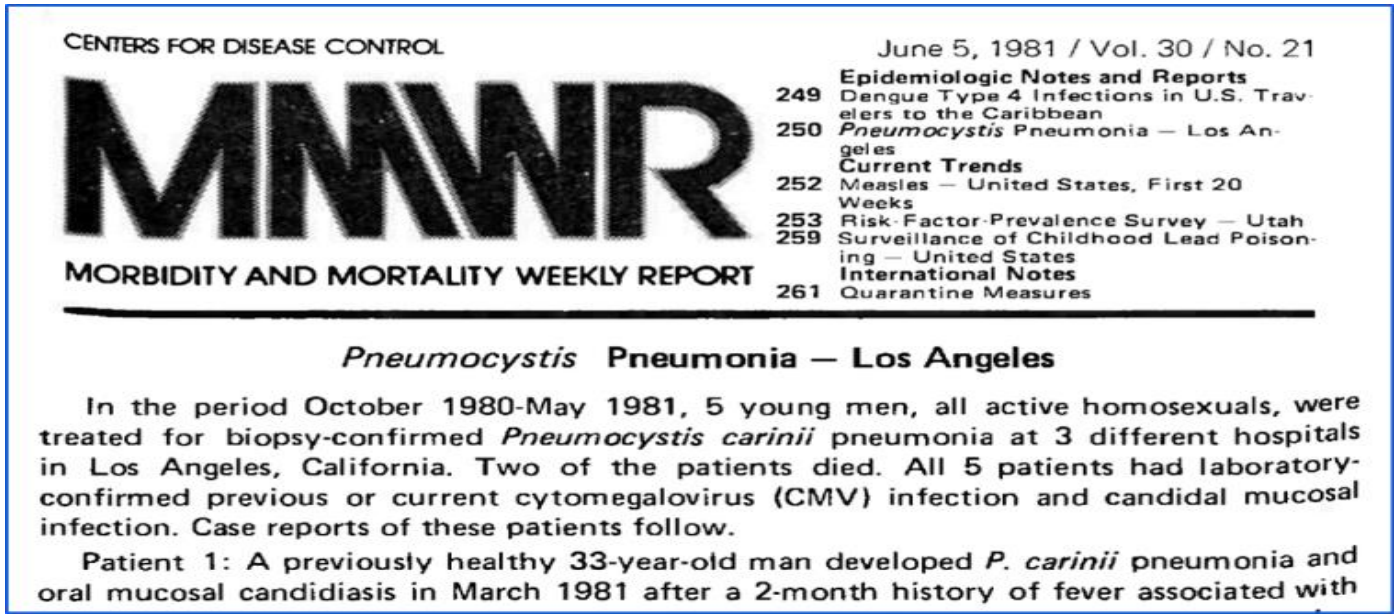
The Lawson Unit
LEADING HIV CARE FOR BRIGHTON

Brighton and Sussex University Hospitals NHS Trust

Introduction

- Set the scene
- What does living with HIV mean in 2018
- How has our conception advice over the years?
  - Evidence base
  - Observations
- Conception
- HIV in Pregnancy
- Contraception

“Document zero”



CENTERS FOR DISEASE CONTROL

June 5, 1981 / Vol. 30 / No. 21

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

Pneumocystis Pneumonia — Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with

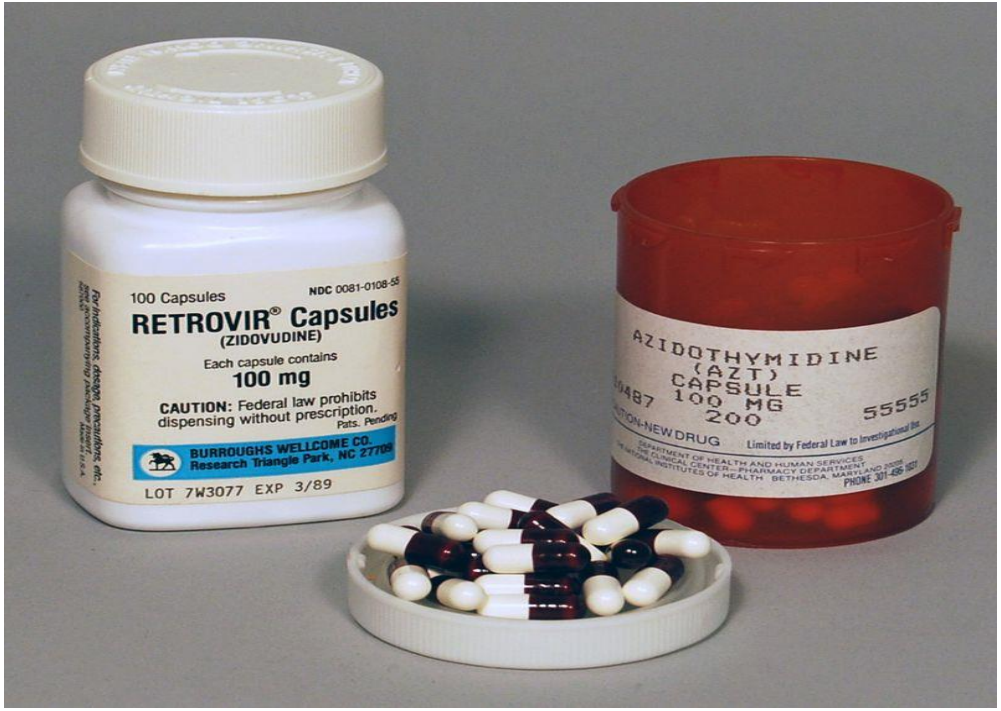
MMWR, 1981; 30: 250-2

Timeline

- 1982:
  - Terry Higgins dies, July 4, St. Thomas' Hospital
- 1983:
  - Terrence Higgins Trust set up, August
  - HIV grown in culture, November
- 1984:
  - HIV the cause of AIDS, April
- 1985:
  - First HIV antibody test

The early days….

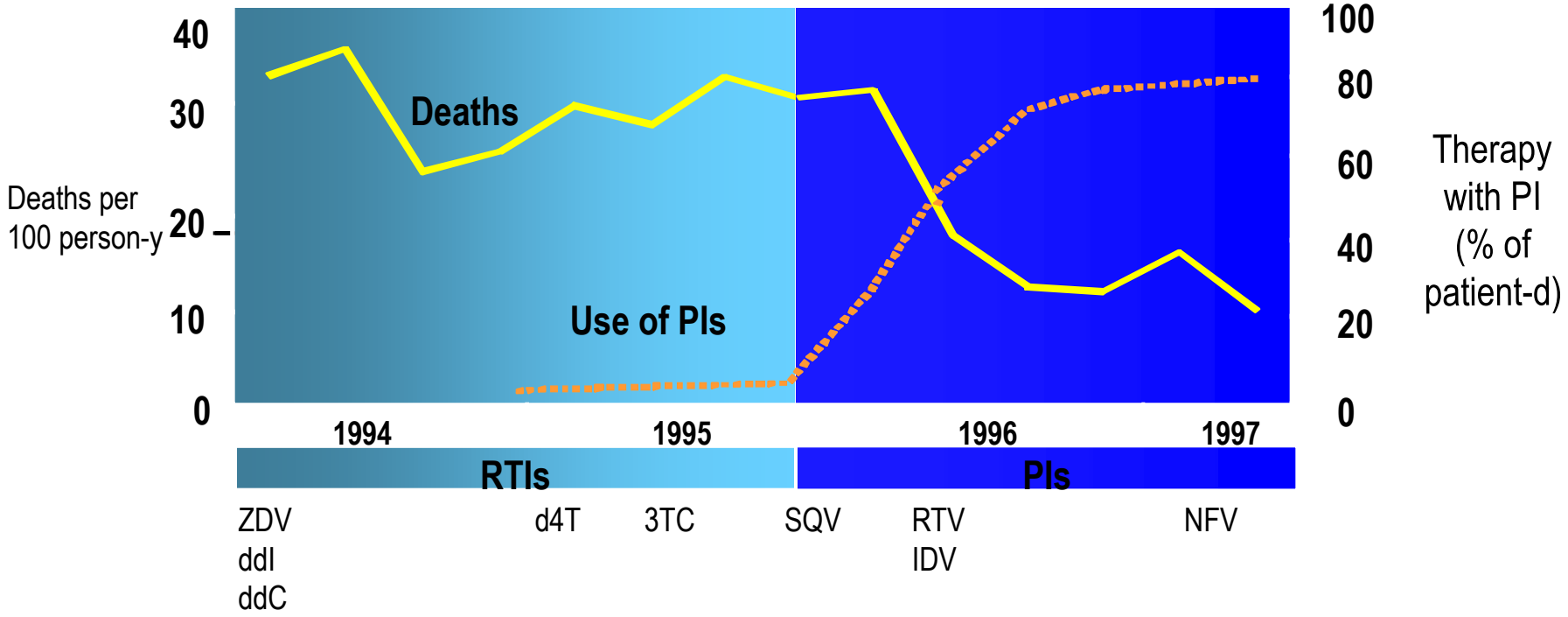
1987


100 Capsules
NDC 0081-0108-55
RETROVIR® Capsules
(ZIDOVUDINE)
Each capsule contains
100 mg
CAUTION: Federal law prohibits dispensing without prescription.
Pats. Pending
BURROUGHS WELLCOME CO.
Research Triangle Park, NC 27709
LOT 7W3077 EXP 3/89
AZIDOTHYMIDINE
(AZT)
CAPSULE
100 MG
200
55555
Limited by Federal Law to Investigational Use

1996: *Everything changed*

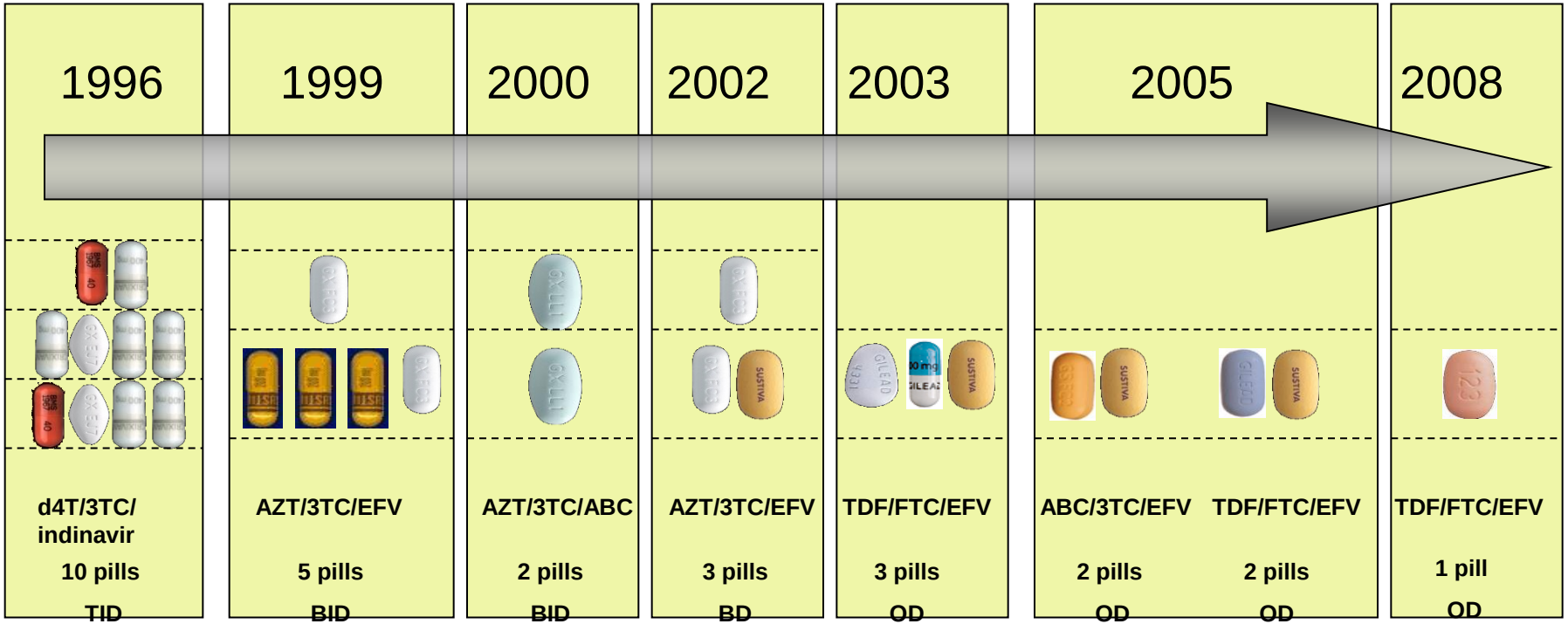
- Vancouver conference
  - protease inhibitors
  - triple therapy or “HAART”
  - viral load testing

Decline in Mortality Rates With Increased Use of PIs



From a cohort of 1255 patients with CD4 counts <100 cells/μL.
Palella FJ Jr et al. *N Engl J Med*. 1998;338:853–860.

Evolution of simpler HAART regimens



2017: "Single-tablet regimens" - 8 currently approved

Antiretroviral drugs 2018

Nucleosides	Nucleotides	NNRTIs	PIs	Fusion inhibitors	Integrase inhibitors	CCR5 antagonists
Zidovudine	Tenofovir	*Delavirdine*	Saquinavir	Enfuvirtide	*Raltegravir*	*Maraviroc*
Zalcitabine	TAF	Nevirapine	Indinavir		Elvitegravir	Vicriviroc
Didanosine		Efavirenz	Ritonavir		Dolutegravir	
Lamivudine		*Etravirine*	Nelfinavir			
Stavudine		Rilpivirine	Fosamprenavir			
Abacavir			Lopinavir			
Emtricitabine			Atazanavir		Booster	
			Tipranavir		Cobicistat	
Combivir®			Darunavir			
Kivexa®						
Truvada®					**Odefsy**	**Juluca**
Atripla	**Stribild**	**Eviplera**	**Triumeq**	**Descovy**	**Genvoya**	**Symtuza**

OPEN

Impact on life expectancy of HIV-1 positive individuals of CD4$^+$ cell count and viral load response to antiretroviral therapy

Margaret T. May[a], Mark Gompels[b], Valerie Delpech[c], Kholoud Porter[d], Chloe Orkin[e], Stephen Kegg[f], Phillip Hay[g], Margaret Johnson[h], Adrian Palfreeman[i], Richard Gilson[j], David Chadwick[k], Fabiola Martin[l], Teresa Hill[m], John Walsh[n], Frank Post[o], Martin Fisher[p], Jonathan Ainsworth[q], Sophie Jose[m], Clifford Leen[r], Mark Nelson[s], Jane Anderson[t], Caroline Sabin[m], for the UK Collaborative HIV Cohort (UK CHIC) Study

Objective: The objective of this study is to estimate life expectancies of HIV-positive patients conditional on response to antiretroviral therapy (ART).

Methods: Patients aged more than 20 years who started ART during 2000–2010 (excluding IDU) in HIV clinics contributing to the UK CHIC Study were followed for mortality until 2012. We determined the latest CD4$^+$ cell count and viral load before ART and in each of years 1–5 of ART. For each duration of ART, lifetables based on estimated mortality rates by sex, age, latest CD4$^+$ cell count and viral suppression (HIV-1 RNA <400 copies/ml), were used to estimate expected age at death for ages 20–85 years.

Results: Of 21 388 patients who started ART, 961 (4.5%) died during 110 697 person-years. At start of ART, expected age at death [95% confidence interval (CI)] of 35-year-old men with CD4$^+$ cell count less than 200, 200–349, at least 350 cells/μl was 71 (68–73), 78 (74–82) and 77 (72–81) years, respectively, compared with 78 years for men in the general UK population. Thirty-five-year-old men who increased their CD4$^+$ cell count in the first year of ART from less than 200 to 200–349 or at least 350 cells/μl and achieved viral suppression gained 7 and 10 years, respectively. After 5 years on ART, expected age at death of 35-year-old men varied from 54 (48–61) (CD4$^+$ cell count <200 cells/μl and no viral suppression) to 80 (76–83) years (CD4$^+$ cell count ≥350 cells/μl and viral suppression).

Conclusion: Successfully treated HIV-positive individuals have a normal life expectancy. Patients who started ART with a low CD4$^+$ cell count significantly improve their life expectancy if they have a good CD4$^+$ cell count response and undetectable viral load.

AIDS 2014, **28**:1193–1202

Correspondence to Dr Margaret T. May, School of Social and Community Medicine, University of Bristol, Bristol BS8 2PS, UK.
Tel: +44 117 9287287; fax: +44 117 928 7325; e-mail: m.t.may@bristol.ac.uk

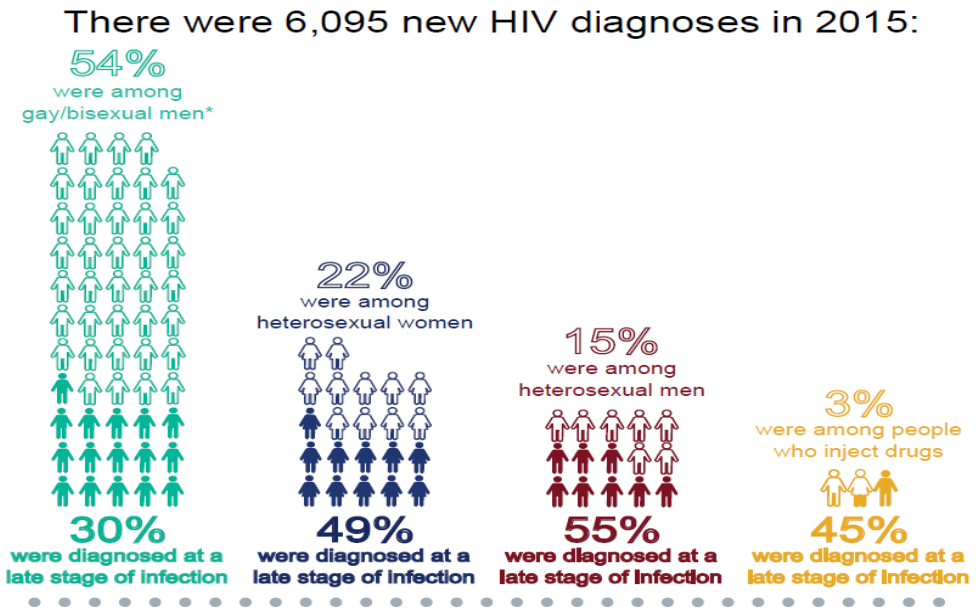
Received: 24 October 2013; revised: 31 January 2014; accepted: 31 January 2014.

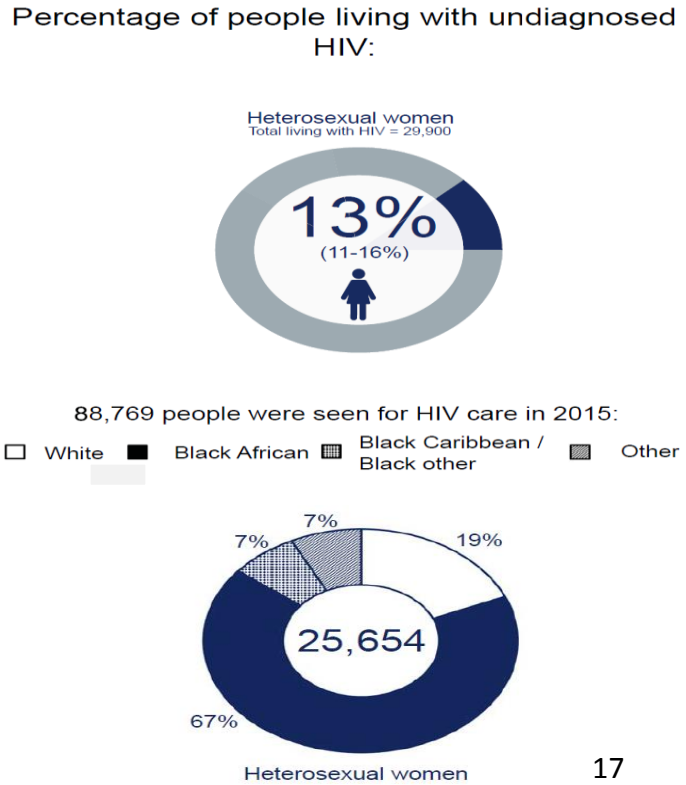
DOI:10.1097/QAD.0000000000000243

ISSN 0269-9370

UK Epidemiology

Public Health England





HIV in the United Kingdom, Infographic HIV 2016, Public Health England. Accessed Aug 17
https://www.gov.uk/government/publications/hiv-in-the-united-kingdom

Attitudes to Pregnancy Pre HAART

- Reproductive possibilities were much restricted in the first years of the HIV pandemic
  - Centers for Disease Control and Prevention (CDC) ***discouraged*** pregnancy in HIV-infected persons due to the poor prognosis of the disease and the risk of transmission to the neonate
  - American College of Obstetrics and Gynaecology, which recommended HIV-infected women ***not*** to become pregnant [1]
  - In 1994 the American Society for Reproductive Medicine suggested other ***alternative options*** such as donor insemination or child adoption
  - HIV-positive individuals continued to seek pregnancy, assuming the risk of sexual and/or vertical transmission of HIV [2]

1. Kass, et al, 1994. 2. Selwyn, et al. 1987

Attitudes to Pregnancy Post HAART

- In 2001 CDC revised their advice stating
  - “healthcare professionals should ‘provide information and give support to any reproductive option for HIV-positive patients', particularly when HIV infection is under medical control”

- The growth in plans for pregnancy among HIV-infected individuals along the HAART era has been highlighted in many reports [1-5]

- In the UK, dedicated guidelines for
  - HIV in Pregnancy, 2001 [6]
  - Sexual and reproductive health, 2008 [6]

1. Riley and Yawetz, 2005. 2. Schuster, et al, 2000. 3. Chen, et al, 2004. 4. Klein, et al, 2003. 5. da Silveira, et al., 2005. 6. www.bhiva.org

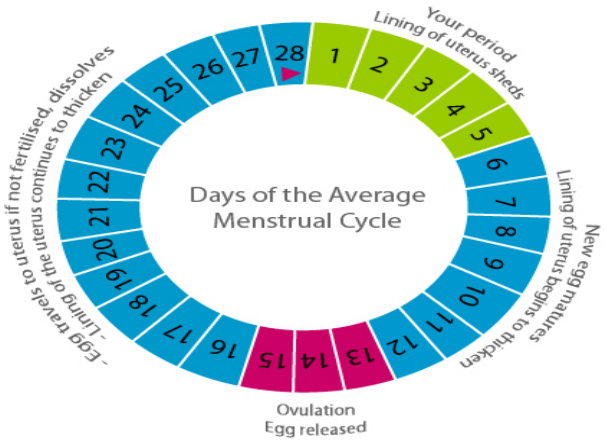
What was known when BHIVA HIV in Pregnancy 2001 Guidelines were written?

- Consistent increased transmission with
  - Mode of delivery
  - Duration of ROM
  - Premature delivery <34 weeks
- Invasive procedures were thought to increase risk of MTCT therefore advised to avoid
- Treatment was routinely stopped after delivery in women with CD4 counts >350 cells/mm3

Preconception advice

Menstruation

- Conflicting data
- May have normal[1] or irregular cycles[2]
- Menstrual abnormalities associated with
  - Low BMI
  - CD4 <200 cells/mm^3
  - High HIV VL >100,000 c/ml
  - Substance misuse



1. Cejtin HE et al. Effects if human immunodeficiency virus on protracted amenorrhea and ovarian dysfunction. Obstet Gynecol 2006;108:1423-1431.
2. Harlow SD et al. Effect of HIV infection on menstrual cycle length. JAIDS 2000;24:68-75.

Image taken from http://www.creaconceptions.com/conception.php Accessed Aug 17

HIV: Reproductive options 2001

HIV+ woman & HIV- man

- Insemination of partner's sperm at ovulation (whether or not on ARVs/ detectable viral load)
- Assisted reproduction in case of fertility disorders
- Adoption

HIV+ man & HIV- woman

- IUI, IVF or ICSI following sperm washing
- Insemination of donor sperm at ovulation
- Adoption

HIV+ man & HIV+ woman

- Natural conception (if effective viral suppression) timed ovulatory intercourse only
- Insemination of sperm at ovulation
- Adoption

What has changed this advice?

- Patients' desires for natural conception
- Swiss statement 2008
- HPTN 052
- Partners in Prevention
- Partner Study

Natural Pregnancy

- Increasing number of requests in both HIV concordant couples and HIV discordant couples (HIV + male)
- Many reasons
  - Cost
  - Failure of ART
    - Up to 30% of couples drop out before starting insemination
    - 30% may not complete ART
      - Drop-out
      - Failure
    - After ART completed but failed – natural attempts reported to be as high as 50% in one cohort[1]
  - Swiss statement
  - PrEP

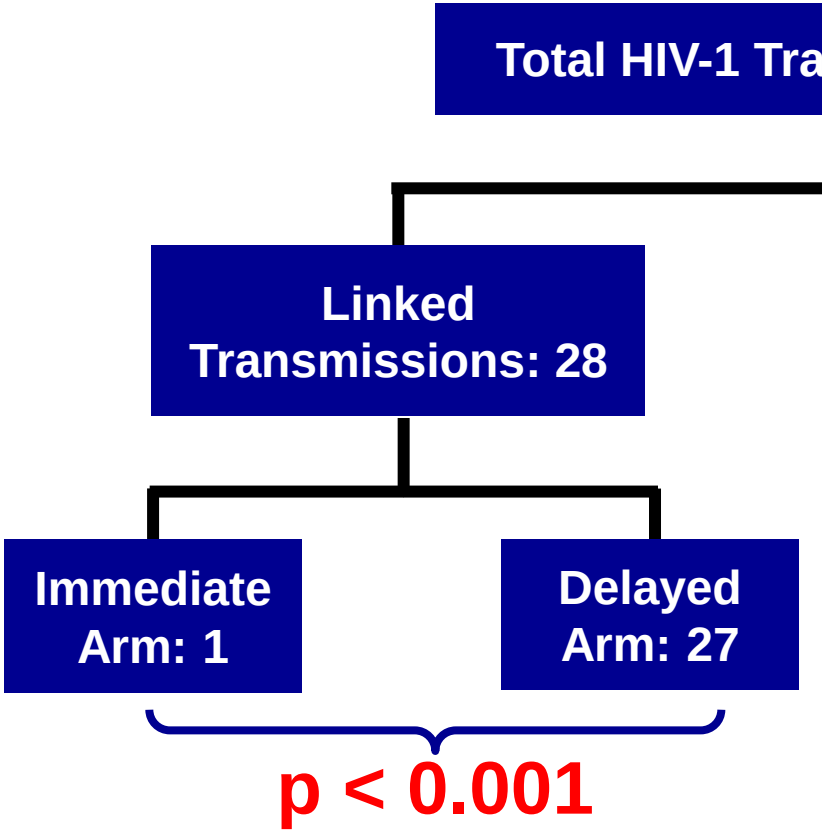
Brighton and Sussex University Hospitals NHS Trust

1. Vernazza et al, 2006 .

Swiss Statement

"An HIV infected individual without an additional STD and on antiretroviral therapy with completely suppressed viraemia is sexually non-infectious i.e. he/she does not pass on HIV through sexual contact"

HPTN 052: HIV-1 Transmission



- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm^3
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

BASHH PEPSE Guidelines 2015

Table 4 Situations when post-exposure prophylaxis (PEP) is considered (IV, grade C)

	Source HIV status			
	HIV-positive		Unknown from high prevalence group/area*	Unknown from low prevalence group/area
	Viral load detectable	Viral load undetectable		
Receptive anal sex	Recommend	Not recommended	Recommend	Not recommended
Insertive anal sex	Recommend	Not recommended	Consider†	Not recommended
Receptive vaginal sex	Recommend	Not recommended	Consider†	Not recommended
Insertive vaginal sex	Recommend	Not recommended	Consider†	Not recommended
Fellatio with ejaculation‡	Consider	Not recommended	Not recommended	Not recommended
Fellatio without ejaculation‡	Not recommended	Not recommended	Not recommended	Not recommended
Splash of semen into eye	Consider	Not recommended	Not recommended	Not recommended
Cunnilingus	Not recommended	Not recommended	Not recommended	Not recommended
Sharing of injecting equipment	Recommended	Not recommended	Consider	Not recommended
Human bite§	Not recommended	Not recommended	Not recommended	Not recommended
Needlestick from a discarded needle in the community			Not recommended	Not recommended

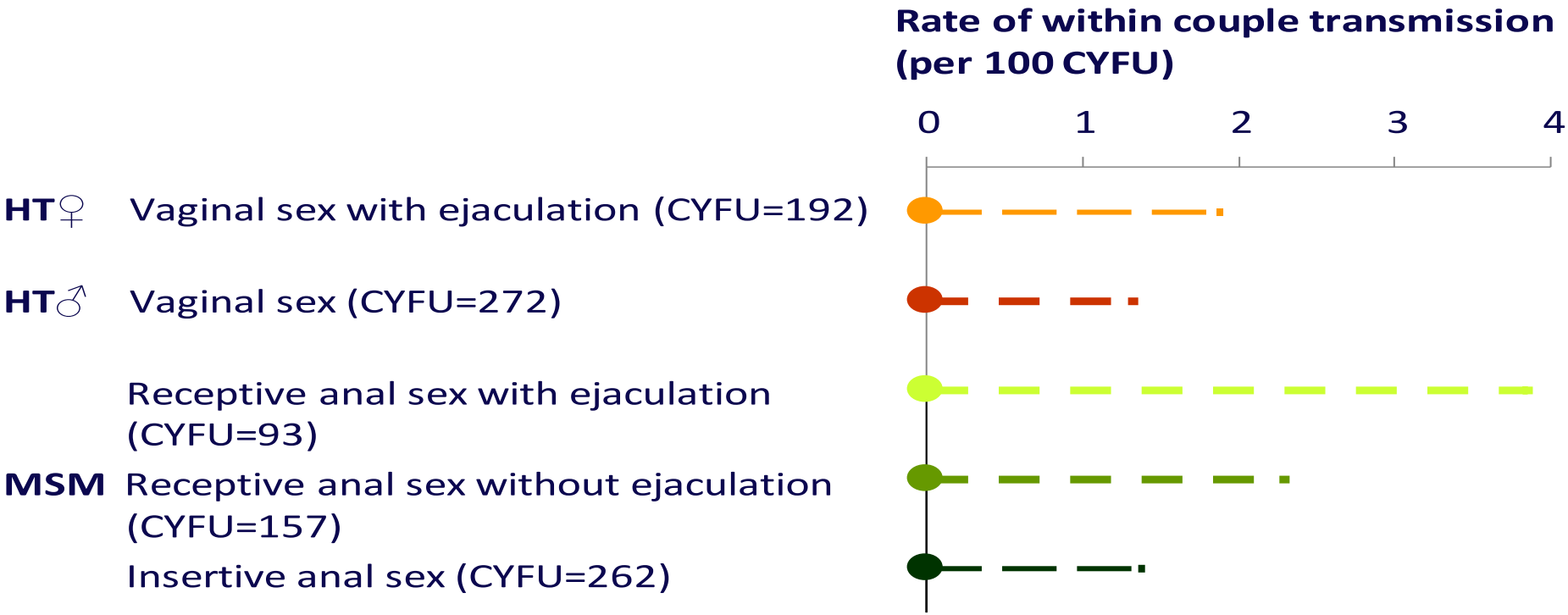
Not recommended

*High prevalence groups within this recommendation are those where there is a significant likelihood of the source individual being HIV-positive. Within the UK at present, this is likely to be men who have sex with men and individuals who have immigrated to the UK from areas of high HIV prevalence (particularly sub-Saharan Africa)
†More detailed knowledge of local prevalence of HIV within communities may change these recommendations from *consider* to *recommended* in areas of particularly high HIV prevalence
‡PEP is not recommended for individuals receiving fellatio i.e. inserting their penis into another's oral cavity
§A bite is assumed to constitute breakage of the skin with passage of blood

HIV: Reproductive options 2015

HIV+ woman & HIV- man
• Treatment of woman to VL<40c/ml then UPSI • PrEP-C • Insemination of partner's sperm at ovulation (whether or not on ARVs/ detectable viral load) • Assisted reproduction in case of fertility disorders • Adoption
HIV+ man & HIV- woman
•Treatment of woman to VL<40c/ml then UPSI •PrEP-C • IUI, IVF or ICSI following sperm washing • Insemination of donor sperm at ovulation • Adoption
HIV+ man & HIV+ woman
• Natural conception (if effective viral suppression) • Insemination of sperm at ovulation • Adoption

PARTNER Study: Rate of HIV transmission according to sexual behaviour reported by the negative partner

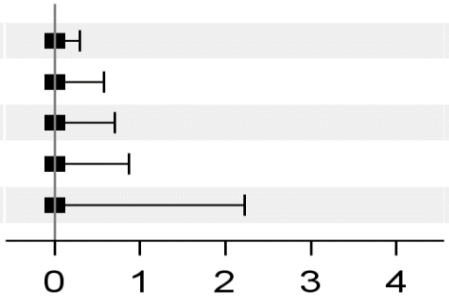


● estimated rate – – 95% confidence interval

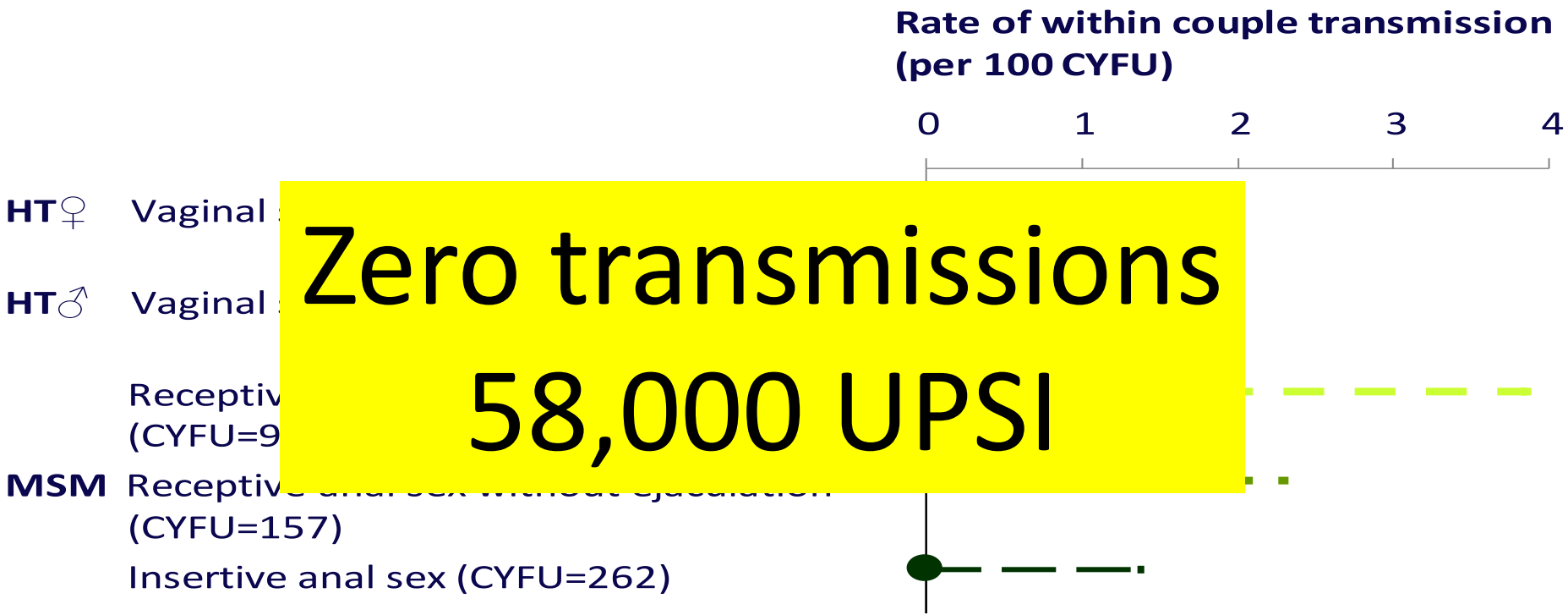
Rodger, CROI 2014

Rate of HIV transmission overall according to sexual behaviour reported by the negative partner – all couples

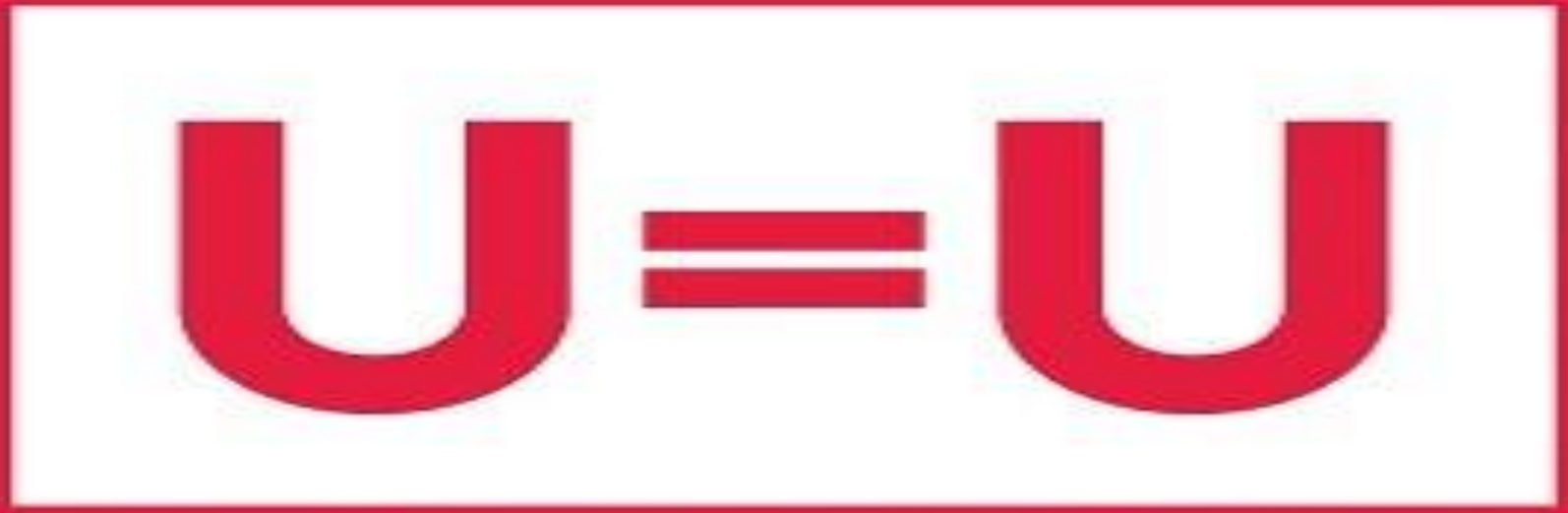
	% of Eligible Couples Reporting Specific Sex Act	Couple-Years of Follow-up	Upper 95% Confidence Limit
Any sex	99.7	1238	0.30
Vaginal sex	60.6	629	0.59
Anal sex	52.9	522	0.71
Insertive anal sex	42.1	417	0.88
Receptive anal sex with ejaculation	21.4	166	2.23



PARTNER Study: Rate of HIV transmission according to sexual behaviour reported by the negative partner



Rodger, CROI 2014



UNDETECTABLE = UNTRANSMITTABLE

HIV: Reproductive options 2018

HIV+ woman & HIV- man

- Treatment of woman to VL<40c/ml then UPSI
- PrEP-C
- Insemination of partner's sperm at ovulation (whether or not on ARVs/ detectable viral load)
- Assisted reproduction in case of fertility disorders
- Adoption

HIV+ man & HIV- woman

- Treatment of woman to VL<40c/ml then UPSI
- PrEP-C
- IUI, IVF or ICSI following sperm washing
- Insemination of donor sperm at ovulation
- Adoption

HIV+ man & HIV+ woman

- Natural conception (if effective viral suppression)
- Insemination of sperm at ovulation
- Adoption

Still work to do with HFEA

- Men with HIV cannot be provided with a surrogate via fertility clin

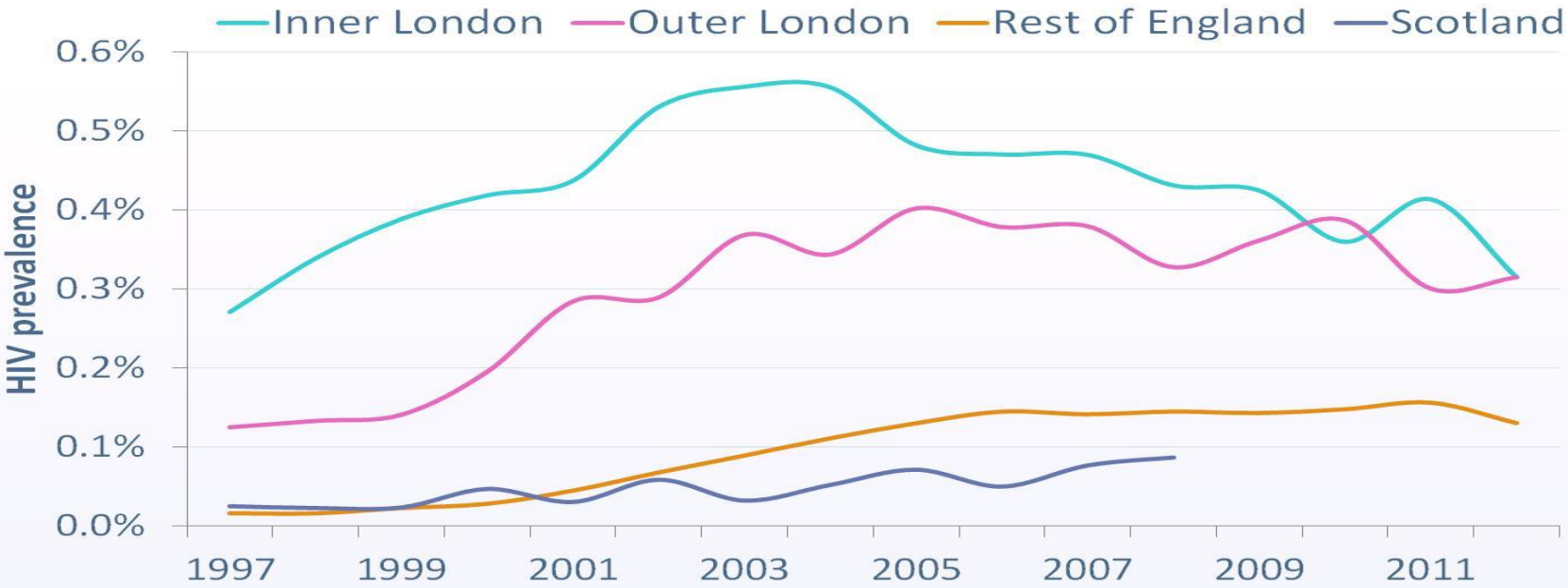
- Women with HIV cannot donate eggs to her partner or anyone else

FSRH Guidelines BHIVA BASHH 2018 will comment on this

HIV in Pregnancy

HIV prevalence among pregnant women

England and Scotland only, 1997-2012 (PHE, HPS and ICH data)

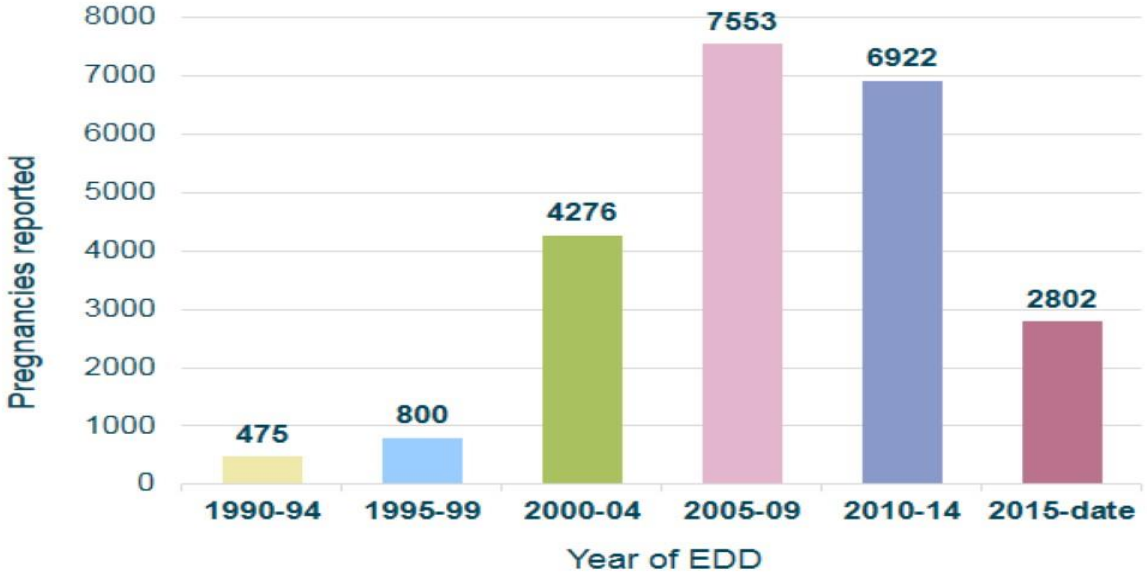


[1]Unlinked anonymous survey of newborn infant dried blood spots, English regions to 2012, & Scotland (to 2008). PHE, HPS and UCL ICH. Included diagnosed *and* undiagnosed women giving birth.

National Study of HIV in Pregnancy and Childhood
NSHPC

Obstetric data snapshot: pregnancies over the years

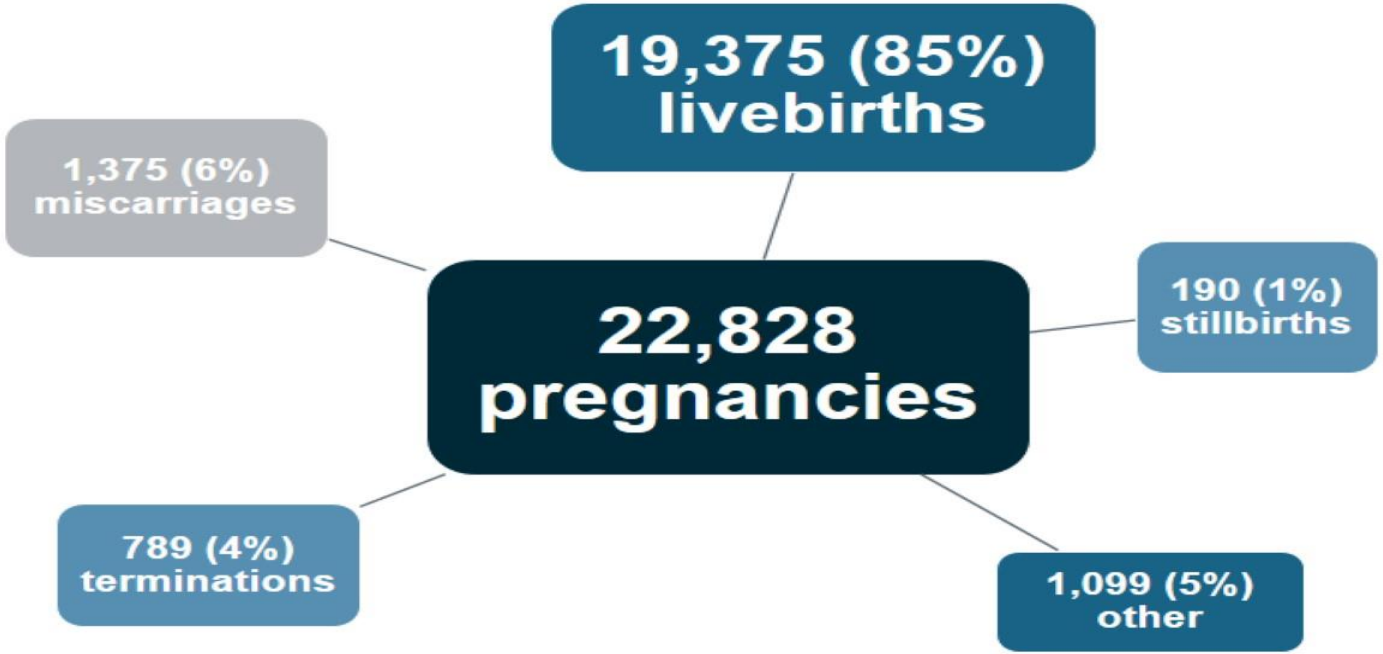
22,828 pregnancies in diagnosed women since 1990 and reported* to the NSHPC by June 2017



Source: pregnancies since 1990 reported to the NSHPC from all sources by June 2017

National Study of HIV in Pregnancy and Childhood
NSHPC

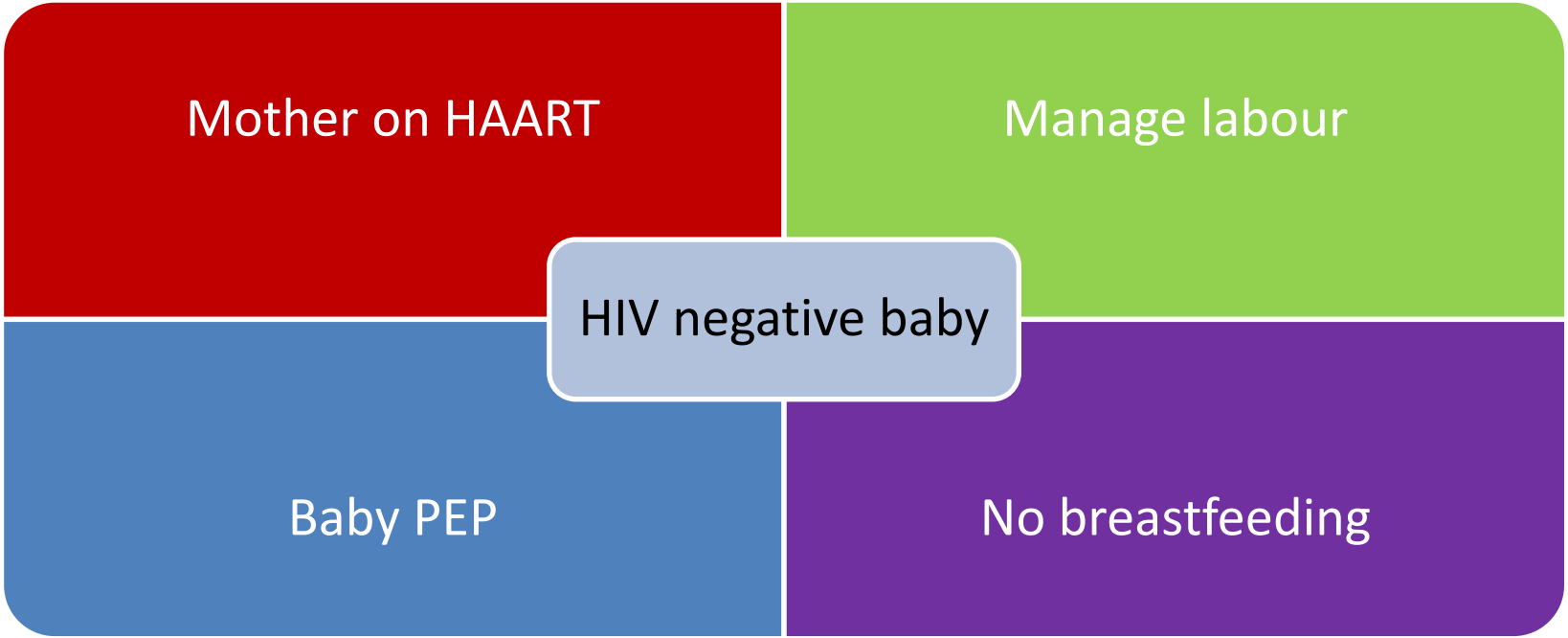
Obstetric data snapshot: pregnancy outcomes



Source: pregnancies since 1990 reported to the NSHPC from all sources by June 2017

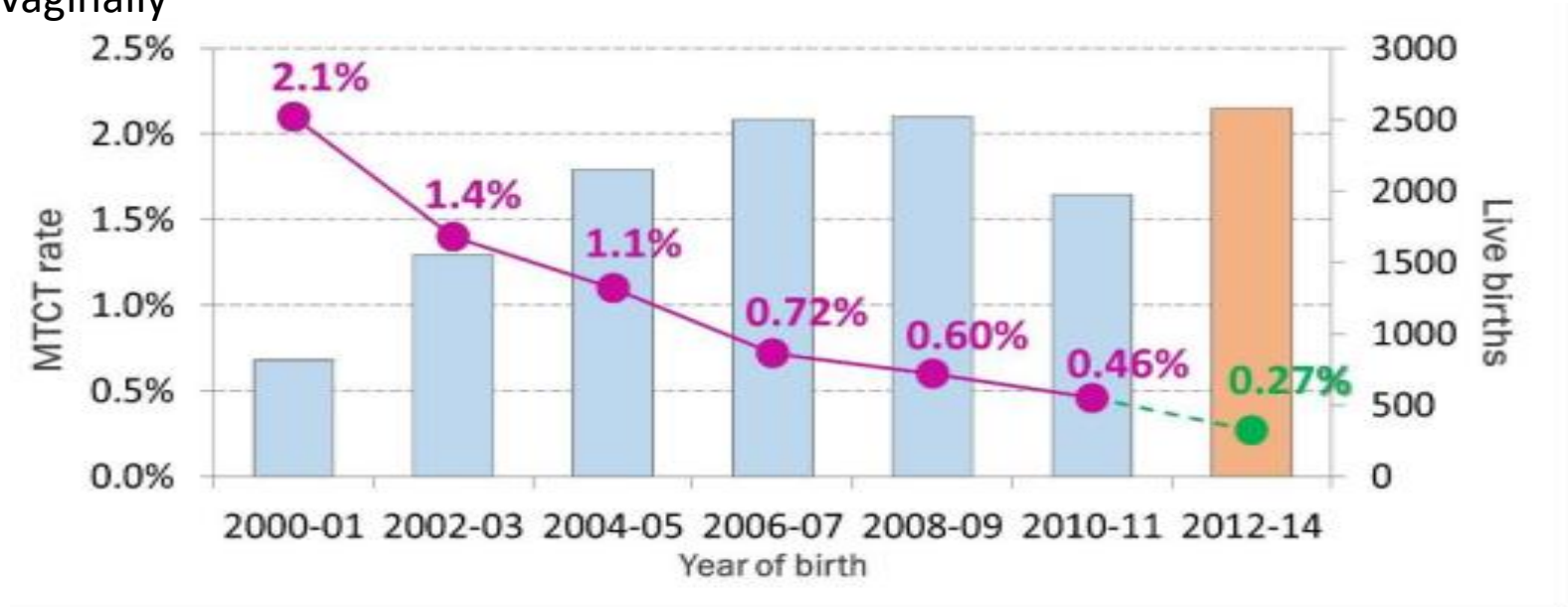
National Study of HIV in Pregnancy and Childhood
NSHPC

Basic principles of HIV in Pregnancy



Mother to Child Transmission in the UK 2016

- Among the **87%** of women delivering with suppressed virus the MTCT rate was **0.14%**
- As a result of high rates of viral suppression nearly half of all women now deliver vaginally



Infection status of children

Born in the **UK** to women diagnosed with HIV before delivery, reported by June 2017*

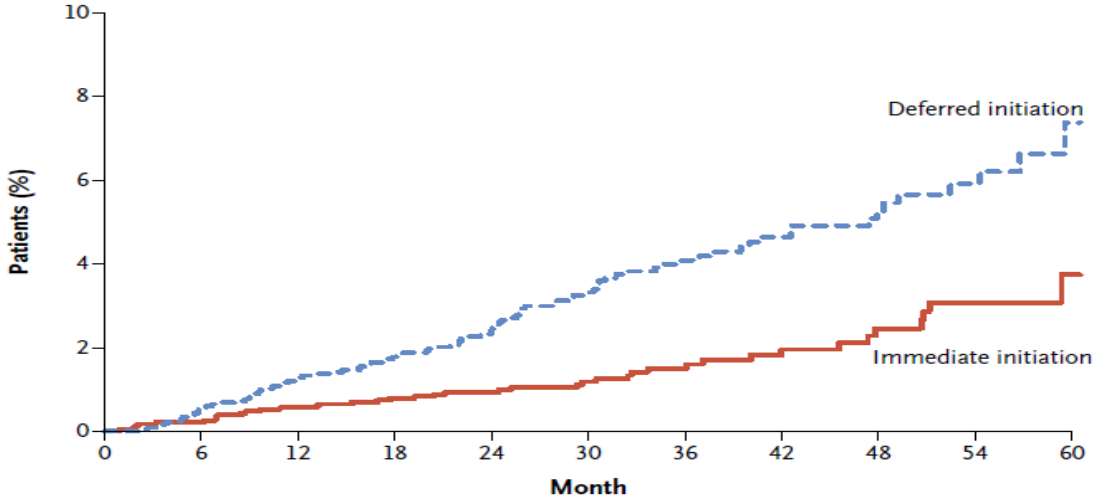
Year of birth	Infected	Indeterminate	Uninfected	Total
Pre 1990	14	19	103	**136**
1990-99	87	117	691	**895**
2000	7	28	293	**328**
2001	6	59	413	**478**
2002	9	51	549	**609**
2003	7	52	804	**863**
2004	9	48	934	**991**
2005	14	51	1058	**1123**
2006	9	52	1125	**1186**
2007	10	57	1228	**1295**
2008	7	53	1214	**1274**
2009	5	73	1186	**1264**
2010	6	67	1254	**1327**
2011	3	121	1067	**1191**
2012	5	83	1078	**1166**
2013	0	140	926	**1066**
2014	3	177	816	**996**
2015	2	390	556	**948**
2016	1	478	353	**832**
2017	0	140	33	**173**
Total	**204**	**2256**	**15681**	**17598**

*760 infected children born to women who were undiagnosed at the time of delivery have also been reported

National Study of HIV in Pregnancy and Childhood
NSHPC

START

A Time to First Primary Event



No. at Risk											
Immediate initiation	2326	2302	2279	2163	1801	1437	1031	757	541	336	110
Deferred initiation	2359	2326	2281	2135	1803	1417	1021	729	520	334	103
Estimated Percentage											
Immediate initiation		0.2	0.6	0.8	0.9	1.2	1.5	2.0	2.5	3.1	3.7
Deferred initiation		0.5	1.2	1.8	2.4	3.3	4.1	4.6	5.3	5.9	7.4

N Engl J Med 2015;373:795-807.

cART and Contraception

- Several ARVs have drug interactions with combined oral contraceptives e.g PIs, NNRTIs and ARVs boosted by cobicistat or ritonavir

- These interactions may decrease or increase blood levels of ethinyl estradiol, norethindrone, or norgestimate and could potentially:
    - Decrease contraceptive efficacy
    - Increase estrogen- or progestin-related adverse effects (e.g thromboembolism)

Contraceptives & HRT Treatment Selector: Liverpool website (www.hiv-druginteractions.org) ***Always refer to the SmPC for full list of DDIs***

		ATV/r	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	RAL	E/C/F/TAF	E/C/F/TDF	NRTI*
Estrogens	Ethinylestradiol	↓19%[a]	↓44%[b]	↓42%[b]	↔[c]	↑22%	↓20%[b]	↑14%	↔	↑3%	↔	↓25%[d]	↓25%[d]	↔
	Estradiol	↓[e]	↓[e]	↓[e]	↓[e]	↓[e]	↓[e]	↔	↔	↔	↔	↑	↑	↔
Progestins	Desogestrel	↑[f,g]	↑[f,g]	↑[f,g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[f,g]	↑[f,g]	↔
	Drospirenone	↑[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Dydrogesterone	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔
	Etonogestrel	↑[g]	↑[g]	↑52%[g]	↓63%[i]	↓[i]	↓[i]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Gestodene	↑[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Levonorgestrel	↑[g]	↑[g]	↑[g]	↓[i]	↓[i]	↓[i]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Medroxy-progesterone (IM)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Medroxy-progesterone (oral)	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔
	Norelgestromin	↑[j]	↑[j]	↑83% [j]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[j]	↑[j]	↔
	Norethisterone (Norethindrone)	↓[h,k]	↓14%[h]	↓17%[h]	↓[h]	↓5%	↓19%[h]	↓11%	↔	↔	↔	↑[g]	↑[g]	↔
	Norgestimate	↑85%[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↑14%	↑126%[g]	↑126%[g]	↔
	Norgestrel	↑[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[g]	↑[g]	↔
Other	Levonorgestrel (EC)	↑	↑	↑	↓58%[l]	↓[l]	↓[l]	↔	↔	↔	↔	↑	↑	↔
	Mifepristone	↑	↑	↑	↓	↓	↓	⇑	⇑	↔	↔	↑	↑	↔
	Ulipristal	↑	↑	↑	↓[m]	↓[m]	↓[m]	↔	↔	↔	↔	↑	↑	↔

NRTI includes ABC, FTC, 3TC, TDF, ZDV

No clinically significant interaction expected.

These drugs should not be coadministered.

Potential interaction which may require a dosage adjustment or close monitoring.

Potential interaction predicted to be of weak intensity (<2 fold ↑AUC or <50% ↓AUC). No a *priori* dosage adjustment is recommended.

↑ Potential increased exposure of the hormone
↓ Potential decreased exposure of the hormone
↔ No significant effect
⇑ Potential increased exposure of HIV drug
⇓ Potential decreased exposure of HIV drug

a Unboosted ATV increased ethinylestradiol AUC by 48%. Use no more than 30 µg of ethinylestradiol if coadministered with unboosted ATV and at least 35 µg of ethinylestradiol if coadministered with ATV/r.
b Alternative or additional contraceptive measures are recommended or, if used for hormone replacement therapy, monitor for signs of estrogen deficiency.
c No effect on ethinylestradiol exposure, however, levels of coadministered progestin were markedly decreased. A reliable method of barrier contraception must be used in addition to oral contraception.
d European SPC states a hormonal contraceptive should contain at least 30 µg ethinylestradiol.
e Monitor for signs of estrogen deficiency.
f Increased conversion to the active metabolite, etonogestrel.
g When used in a combination pill the estrogen component is reduced. In the absence of clinical data on the contraceptive efficacy, caution is recommended contraceptive measures should be used.
h A reliable method of barrier contraception must be used in addition to oral contraception.
i The use of implants or vaginal rings is not recommended in women on long-term treatment with hepatic enzyme-inducing drugs.
j Norelgestromin is administered with ethinylestradiol as a transdermal patch. Ethinylestradiol exposure was reduced which may compromise contraceptive efficac Caution is recommended and additional contraceptive measures should be used.
k Unboosted ATV increased norethisterone AUC by 2.1-fold.
l Use 3 mg as a single dose for emergency contraception. Of note, the doubling of the standard dose is outside the product license and there is limited evidence in relation to efficacy.
m May reduce the efficacy of the emergency contraceptive pill.

www.hiv-druginteractions.org
Accessed Aug 17

Emergency contraception: Copper IUD or Levonelle (LNG EC)

- All women must receive counselling regarding pregnancy and STIs
- Recommended dose Levonelle 1.5g[1] ONCE if no ARVs
- Women using enzyme-inducing drugs or within 28 days of stopping them, should be advised to take a total of 3 mg LNG (two 1.5 mg tablets) as a single dose as soon as possible and within 72 hours of unprotected sex

- Ulipristal acetate (UPA) (EllaOne)[2] is not advised in women using enzyme-inducing drugs or who have taken them within the last 28 days

1. Levonelle SmPC available at www.medicines.org.uk/emc/medicine/16887 Accessed Aug 17
2. ellaOne SmPC available at www.medicines.org.uk/emc/medicine/22280 Accessed Aug 17

Long Acting Contraception

- IUD/IUS work very well for women with HIV
- No clinically significant interactions are expected with these methods and most ARVs
- IUS will also reduce bleeding and dysmenorrhoea
- Depo Provera may be used as in HIV negative women with the same intervals of 12 weeks between injections for women living with HIV
  - Need to consider bone mineral density
- Implanon: cannot use with NNRTIs, Pis or boosters

Contraceptives & HRT Treatment Selector: Liverpool website (www.hiv-druginteractions.org) ***Always refer to the SmPC for full list of DDIs***

		ATV/r	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	RAL	E/C/F/TAF	E/C/F/TDF	NRTI*
Estrogens	Ethinylestradiol	↓19%[a]	↓44%[b]	↓42%[b]	↔[c]	↑22%	↓20%[b]	↑14%	↔	↑3%	↔	↓25%[d]	↓25%[d]	↔
	Estradiol	↓[e]	↓[e]	↓[e]	↓[e]	↓[e]	↓[e]	↔	↔	↔	↔	↑	↑	↔
Progestins	Desogestrel	↑[f,g]	↑[f,g]	↑[f,g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[f,g]	↑[f,g]	↔
	Drospirenone	↑[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Dydrogesterone	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔
	Etonogestrel	↑[g]	↑[g]	↑52%[g]	↓63%[i]	↓[i]	↓[i]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Gestodene	↑[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Levonorgestrel	↑[g]	↑[g]	↑[g]	↓[i]	↓[i]	↓[i]	↔	↔	↔	↔	↑[g]	↑[g]	↔
	Medroxy-progesterone (IM)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Medroxy-progesterone (oral)	↑	↑	↑	↓	↓	↓	↔	↔	↔	↔	↑	↑	↔
	Norelgestromin	↑[j]	↑[j]	↑83% [j]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[j]	↑[j]	↔
	Norethisterone (Norethindrone)	↓[h,k]	↓14%[h]	↓17%[h]	↓[h]	↓5%	↓19%[h]	↓11%	↔	↔	↔	↑[g]	↑[g]	↔
	Norgestimate	↑85%[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↑14%	↑126%[g]	↑126%[g]	↔
	Norgestrel	↑[g]	↑[g]	↑[g]	↓[h]	↓[h]	↓[h]	↔	↔	↔	↔	↑[g]	↑[g]	↔
Other	Levonorgestrel (EC)	↑	↑	↑	↓58%[l]	↓[l]	↓[l]	↔	↔	↔	↔	↑	↑	↔
	Mifepristone	↑	↑	↑	↓	↓	↓	⇑	⇑	↔	↔	↑	↑	↔
	Ulipristal	↑	↑	↑	↓[m]	↓[m]	↓[m]	↔	↔	↔	↔	↑	↑	↔

NRTI includes ABC, FTC, 3TC, TDF, ZDV

No clinically significant interaction expected.

These drugs should not be coadministered.

Potential interaction which may require a dosage adjustment or close monitoring.

Potential interaction predicted to be of weak intensity (<2 fold ↑AUC or <50% ↓AUC). No a *priori* dosage adjustment is recommended.

↑ Potential increased exposure of the hormone
↓ Potential decreased exposure of the hormone
↔ No significant effect
⇑ Potential increased exposure of HIV drug
⇓ Potential decreased exposure of HIV drug

a Unboosted ATV increased ethinylestradiol AUC by 48%. Use no more than 30 µg of ethinylestradiol if coadministered with unboosted ATV and at least 35 µg of ethinylestradiol if coadministered with ATV/r.
b Alternative or additional contraceptive measures are recommended or, if used for hormone replacement therapy, monitor for signs of estrogen deficiency.
c No effect on ethinylestradiol exposure, however, levels of coadministered progestin were markedly decreased. A reliable method of barrier contraception must be used in addition to oral contraception.
d European SPC states a hormonal contraceptive should contain at least 30 µg ethinylestradiol.
e Monitor for signs of estrogen deficiency.
f Increased conversion to the active metabolite, etonogestrel.
g When used in a combination pill the estrogen component is reduced. In the absence of clinical data on the contraceptive efficacy, caution is recommended contraceptive measures should be used.
h A reliable method of barrier contraception must be used in addition to oral contraception.
i The use of implants or vaginal rings is not recommended in women on long-term treatment with hepatic enzyme-inducing drugs.
j Norelgestromin is administered with ethinylestradiol as a transdermal patch. Ethinylestradiol exposure was reduced which may compromise contraceptive efficac Caution is recommended and additional contraceptive measures should be used.
k Unboosted ATV increased norethisterone AUC by 2.1-fold.
l Use 3 mg as a single dose for emergency contraception. Of note, the doubling of the standard dose is outside the product license and there is limited evidence in relation to efficacy.
m May reduce the efficacy of the emergency contraceptive pill.

www.hiv-druginteractions.org
Accessed Aug 17

Summary

- 2018 is an exciting time for HIV, Fertility and Conception
  - Multiple ARVs giving choice to individualise therapy
  - U=U
  - Vertical transmission at lowest rate ever
- But we still have work to do
  - HFEA recommendations regarding surrogacy and egg donation