

Session 5 - Alive and Thriving: Treatment, Care and Support for Adolescents Living with HIV

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Perinatal HIV: your 20s and beyond



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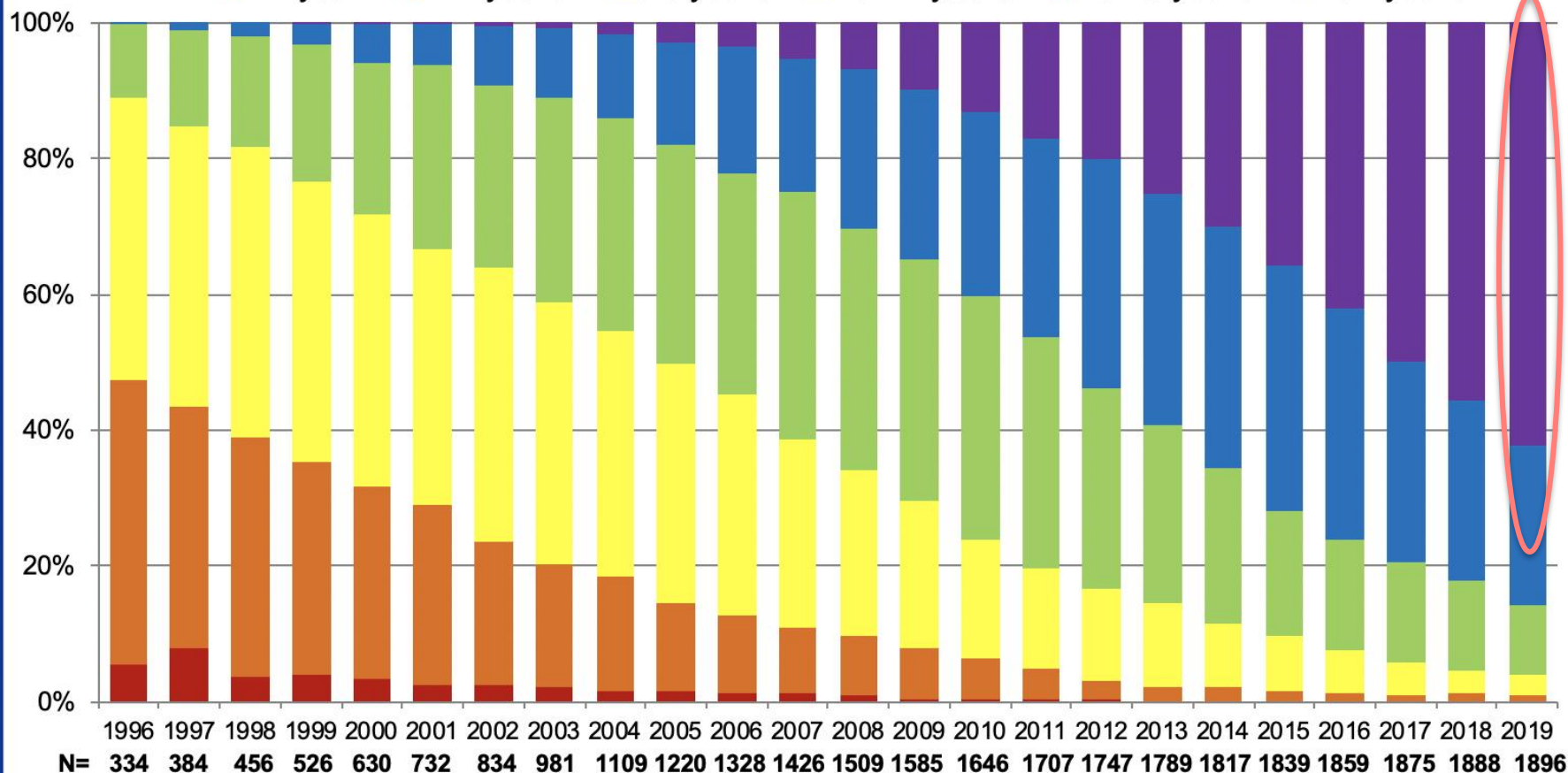
Objectives

- To describe treatment approaches to support young adults living with perinatal HIV to achieve viral suppression.
- To describe the key considerations for fertility/managing pregnancy in young women with perinatal HIV.
- To understand mental health issues faced by adolescents and young adults living with HIV

Age of UK/Irish cohort of patients with HIV acquired in childhood, 1996-2019



■ <1 year
 ■ 1-4 years
 ■ 5-9 years
 ■ 10-14 years
 ■ 15-19 years
 ■ 20+ years



Note: Data are for all children and young people alive who ever presented to medical services in the UK/Ireland, including children who have since transferred to adult care; those who subsequently died or were lost to follow-up are excluded from the year of death or loss to follow-up. All paediatric patients included, from date of first presentation to medical services in the UK, regardless of mode of acquisition (91% perinatal). CHIPS includes all diagnosed HIV-infected children known to be living in the UK/Ireland, of whom 58% were born abroad. Data for 2019 are incomplete as subject to reporting delay. Republic of Ireland ceased reporting in 2018; those reported up to that date are included here.

Mortality and HIV

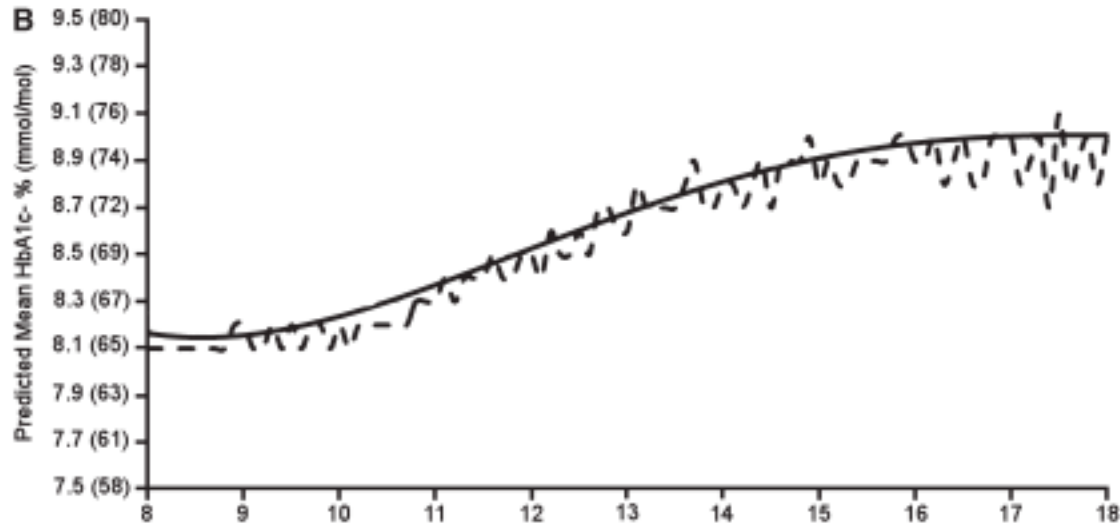
- 15-19 years: Only age group where HIV mortality continues to rise¹
- Outcomes poorer at all stages of the care cascade (diagnosis, retention, access to treatment, viral suppression)² in all settings

¹Slogrove JIAS 2017, ²Enane Curr Op HIV AIDS 2018



Poor adherence is an adolescent norm

Foster, Ayers, Fidler. *Ther Adv Inf Dis* 2020

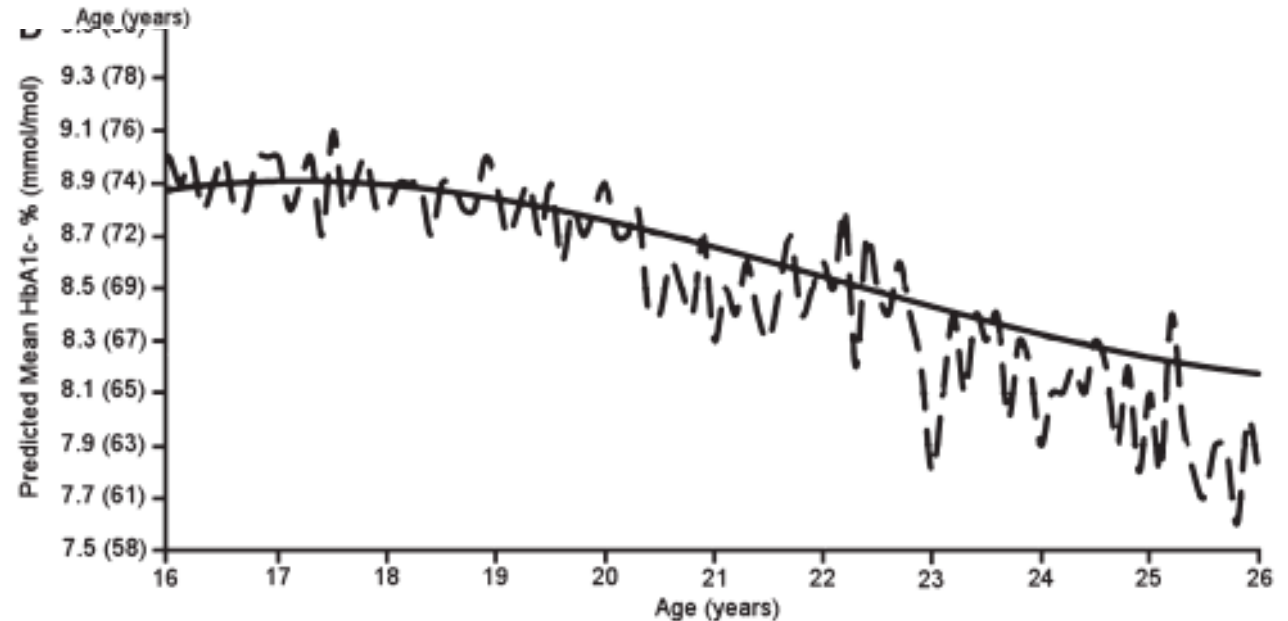


Pediatric Diabetes 2016; 17: 327–336
doi: 10.1111/pedi.12295
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Pediatric Diabetes

Original Article

Hemoglobin A1c (HbA1c) changes over time among adolescent and young adult participants in the T1D exchange clinic registry



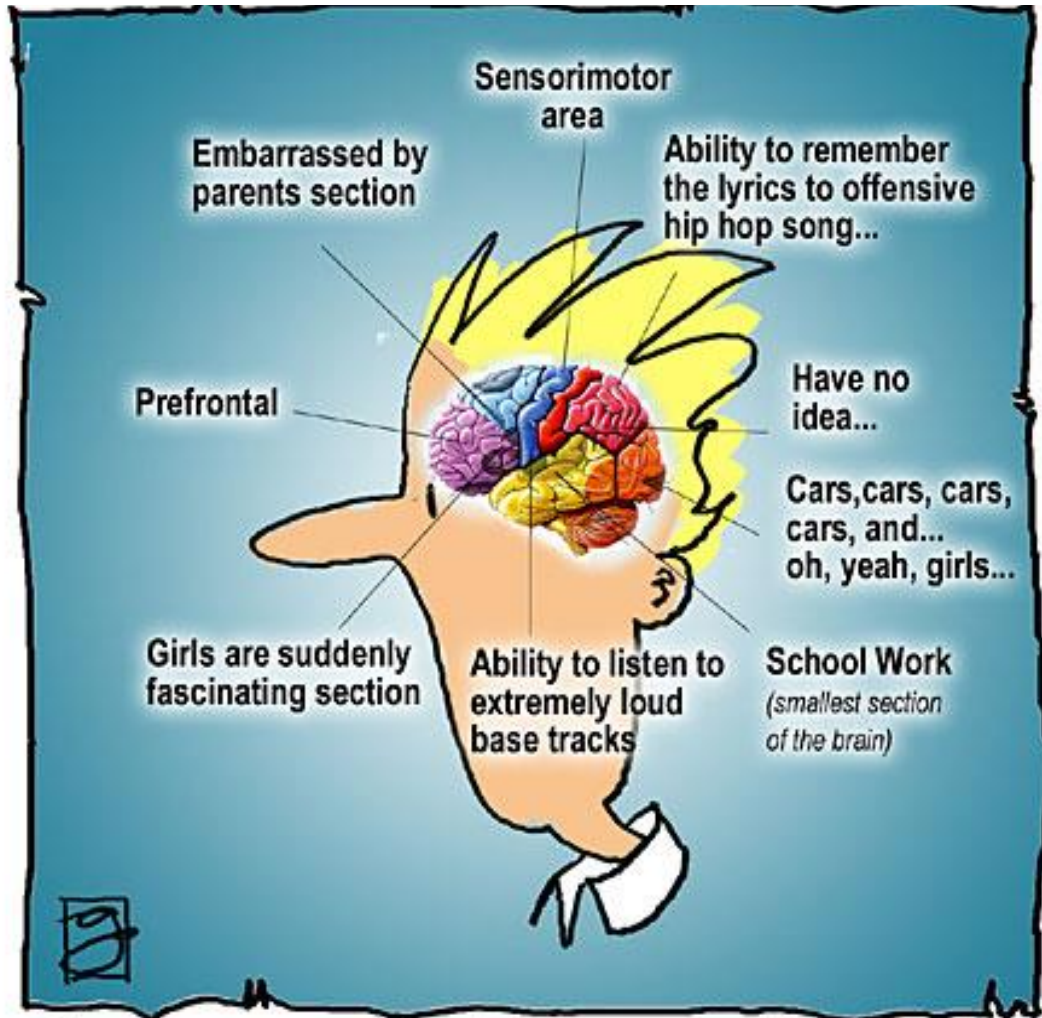
RISK BEHAVIOURS IN YOUTH WITH CHRONIC CONDITIONS

- current smoking 1.32 (1.13, 1.54)
 - illegal drugs 1.49 (1.15, 1.92)
 - early sexual debut 1.33 (1.03, 1.72)
 - eating disorder 1.44 (1.26, 1.74)
 - antisocial acts 1.48 (1.26, 1.74)
 - attempted suicide 2.24 (1.55, 3.24)
-
- more likely to report 3 or > 4 simultaneous behaviours

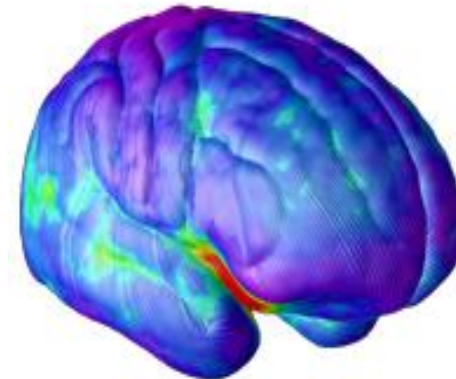
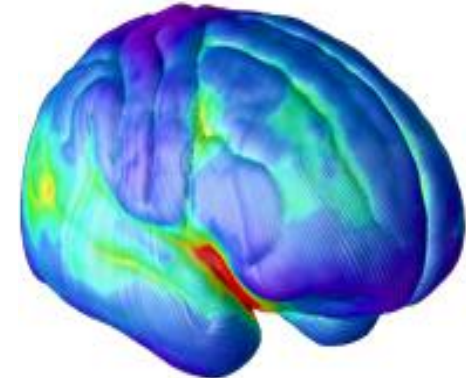
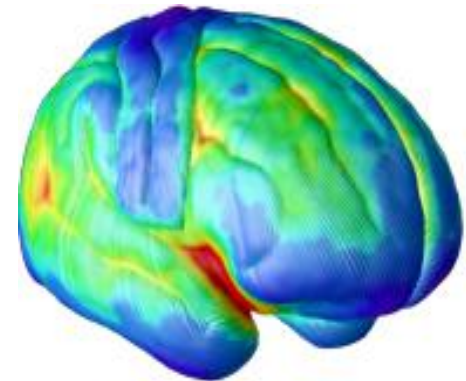
JC Suris et al, 2007 J Begent CHIVA 2010

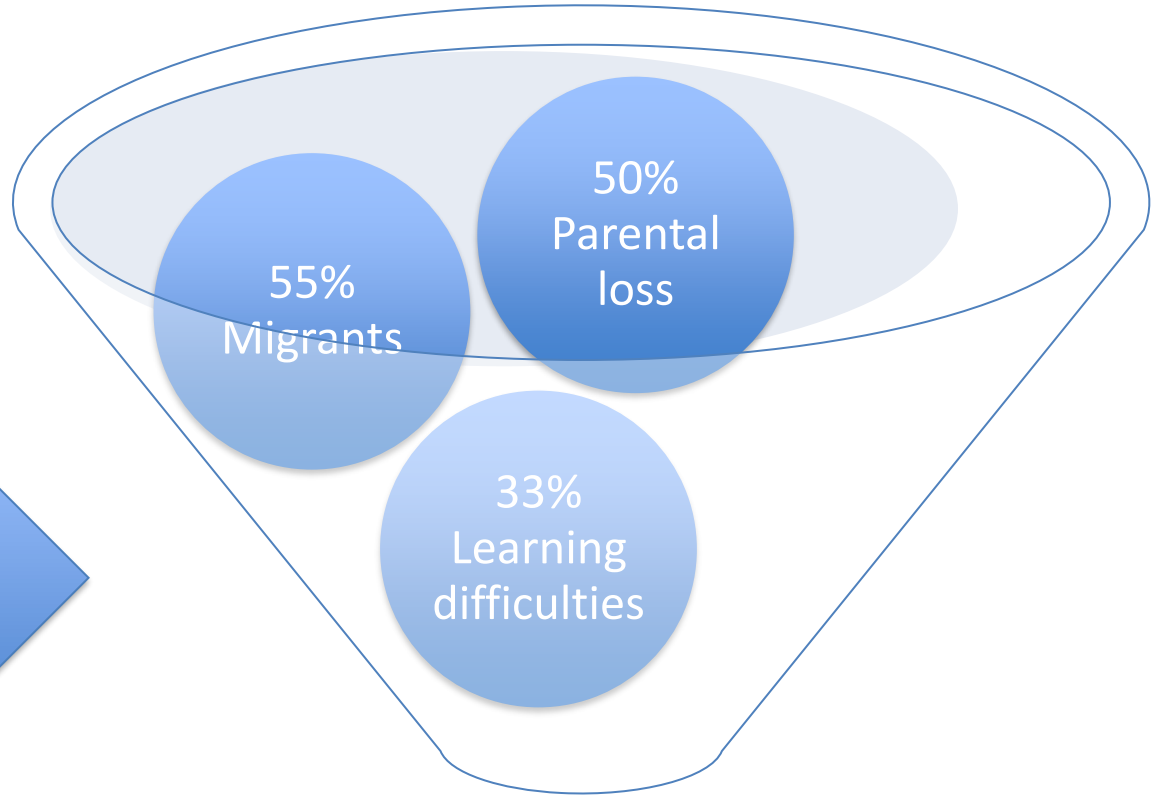
Prefrontal cortex maturation - 3rd decade

impulse control, planning, emotional regulation



Anatomy of a Teenager's Brain





LTFU



Death, onward transmission

Age 15

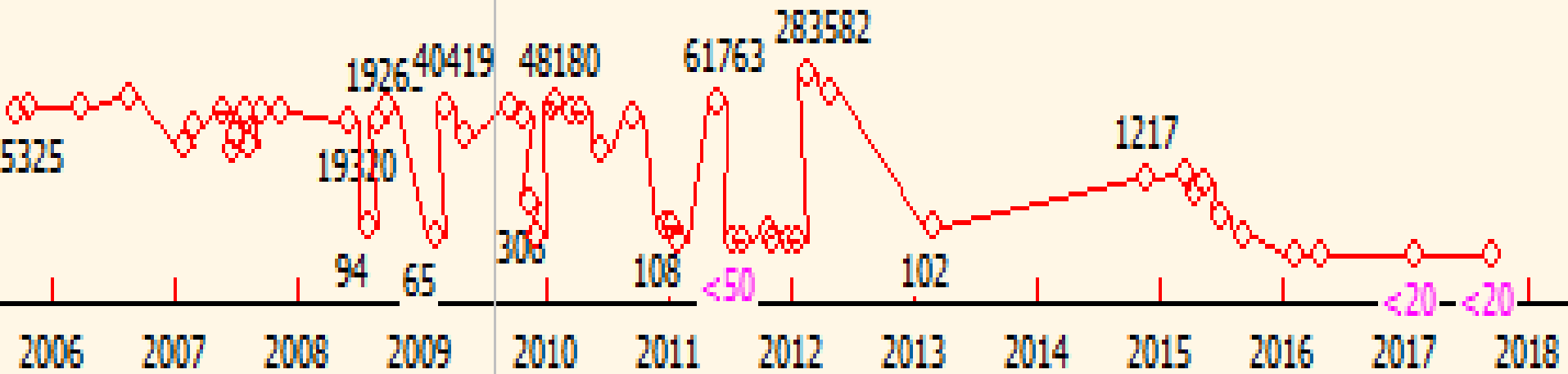
Patience

P1

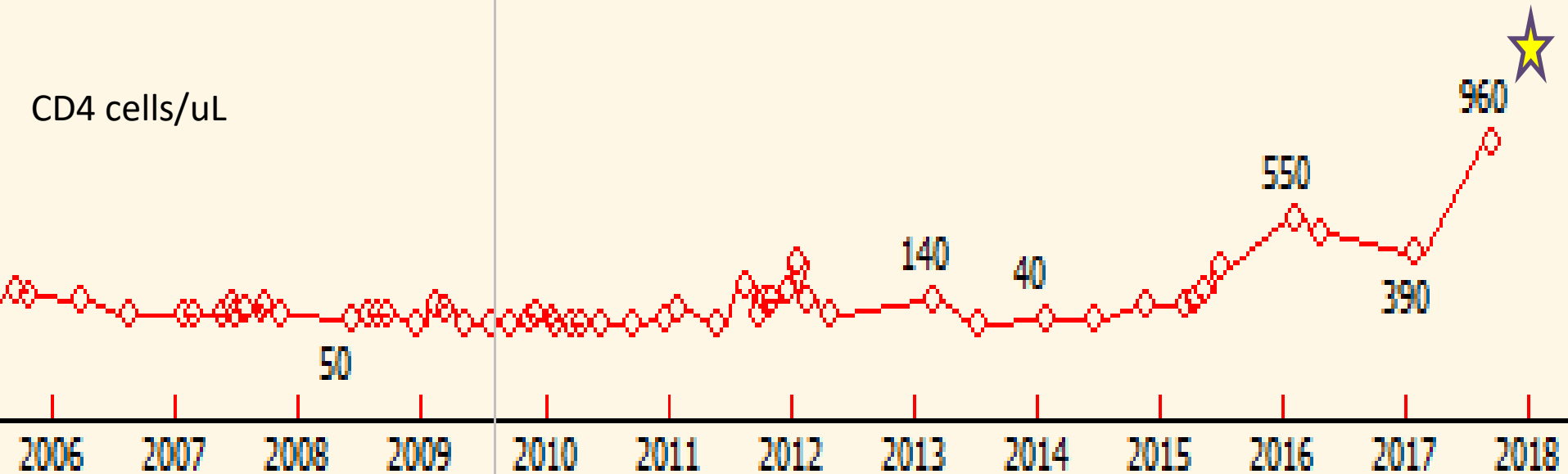
P2

Age 25

HIV VL c/ml



CD4 cells/uL



ADOLESCENTS ARE UNIQUE.

THEY NEED QUALITY HEALTH SERVICES THAT RECOGNIZE THIS

I want to have a say in decisions
about my health

I don't want my parents to know

Please respect my privacy

Don't treat me like a child



Afternoons, **walk in**, MDT, sexual health contraception vaccination, **peer support**, social care, finances, pregnancy and infant testing, “GP care”



Non-judgmental MDT Adherence Support
Clinical Nurse specialist, Psychology, Peer counsellor,
Dietician, Pharmacist, Social Services, Community
Motivational Interviewing communication style
Walk in access to Youth Friendly Service
Transport costs supported

ART
Resistance, Simplification,
Virtual Clinic Referral
High genetic barrier regimen
Pill size/number/formulation,
Pill Glide

SMS support, Hypnosis,
Community DOT
Financial Incentives,
Food chain

Gastrostomy

LA-ART





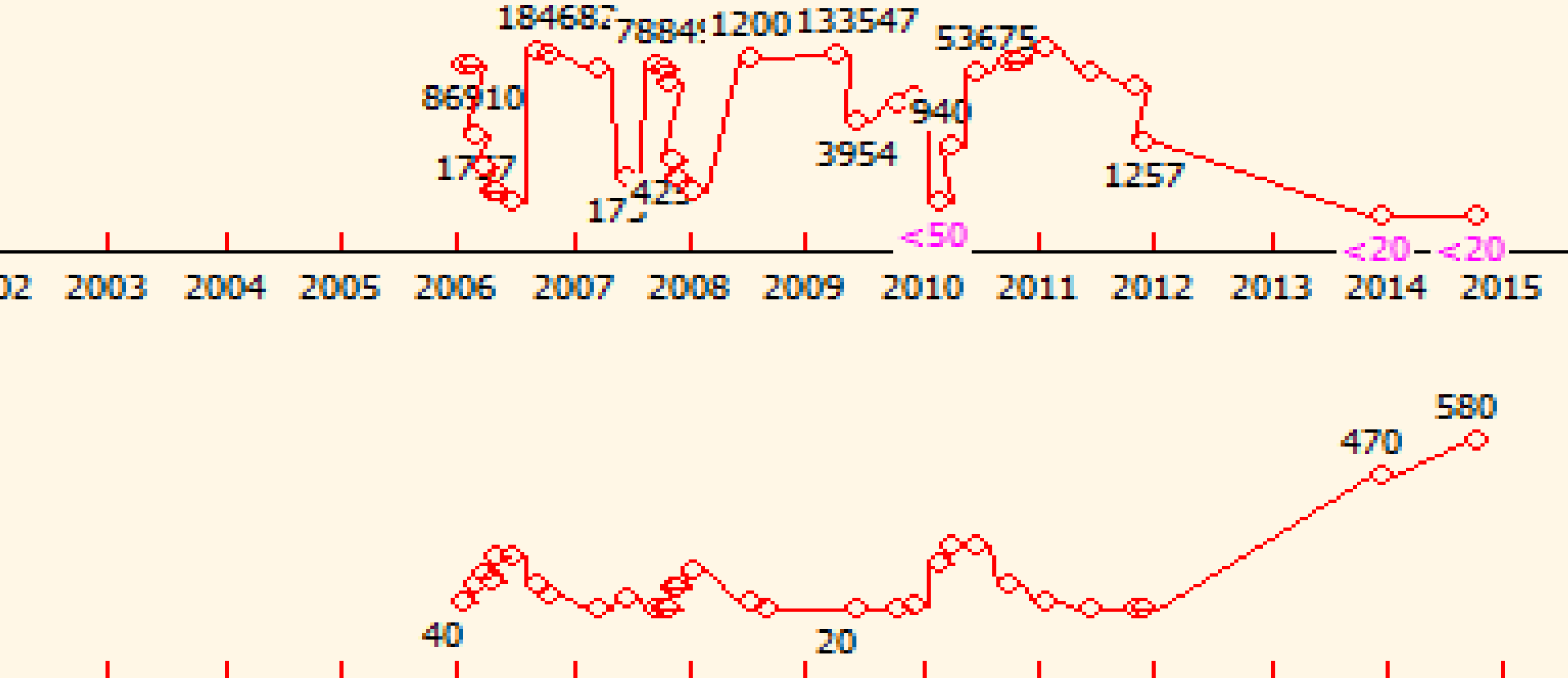
Drug Resistance Interpretation: RT

NRTI Resistance Mutations: **M184I**
 NNRTI Resistance Mutations: None
 Other Mutations: None



Jane age 16: DRV/r/FTC/TDF

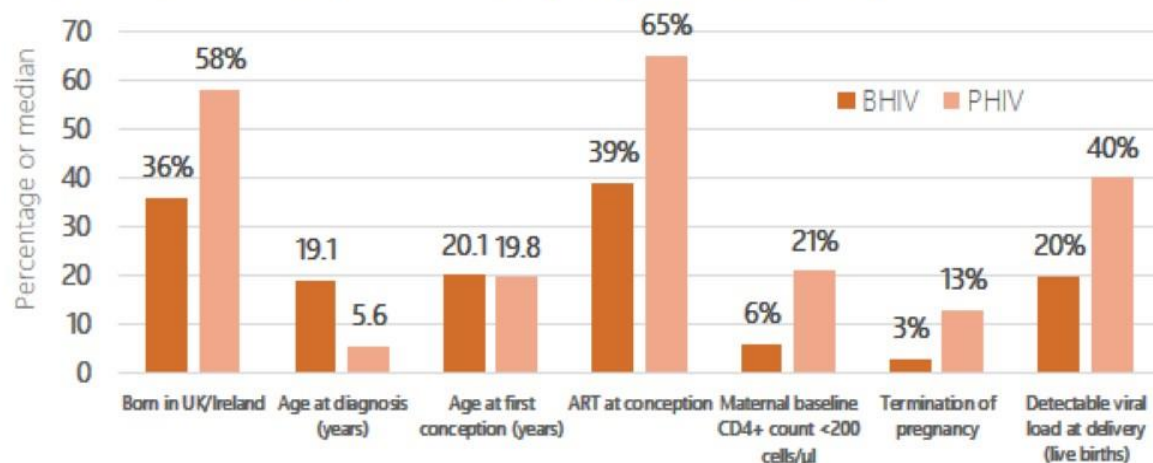
DTG, F/TAF



Pregnancies in women with perinatal HIV (PHIV)

- Of 630 women reported to NSHPC in childhood, 45 (7%) had at least one pregnancy reported
- Pregnancy incidence rate lower in PHIV than in women of similar age in general UK population
- 70 pregnancies among 45 women with PHIV were compared with 184 pregnancies among 118 age-matched women with behaviourally-acquired HIV (BHIV)

13 per 1000 woman-years
pregnancy incidence rate among women with PHIV



Women with PHIV were 3x more likely to have detectable viral load near delivery [OR 3.22 (CI 1.22-8.48)]

For a link to full publication, visit www.ucl.ac.uk/nshpc/publications.

Maternal and pregnancy characteristics, PHIV vs. BHIV (data source: Byrne *et al.* 2017 AIDS)

National Surveillance of HIV in
NSHPC
Pregnancy and Childhood

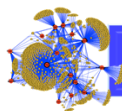
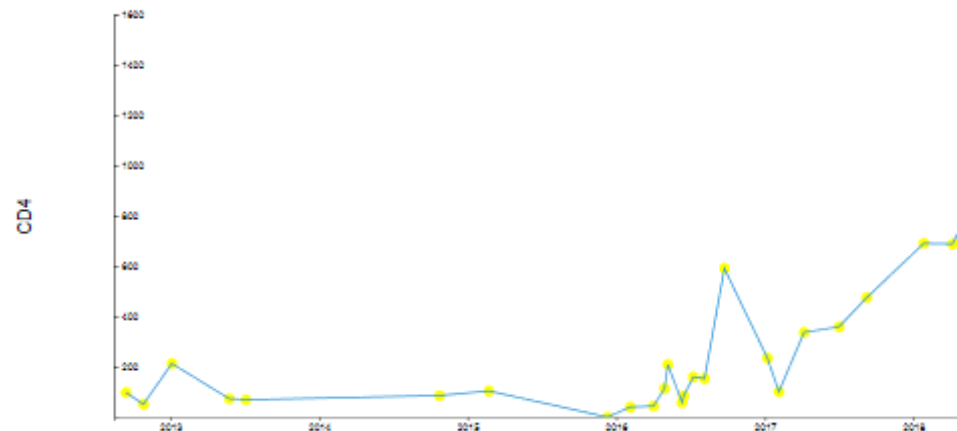
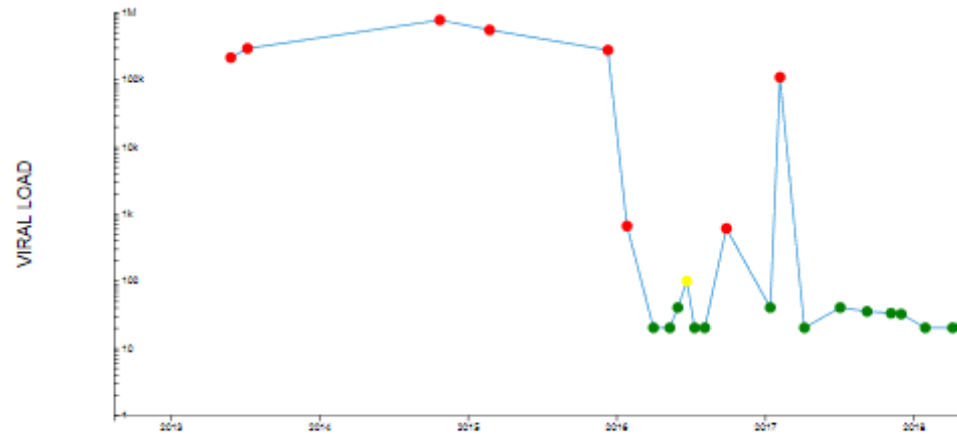
ISSS
Integrated Screening Outcomes Surveillance Service





Pregnancy prescribing: lessons learnt

- 24 year old
- PaHIV
- Prior poor adherence
- Suppressed on DTG/ABC/3TC
- Pregnant 5/40



PVC

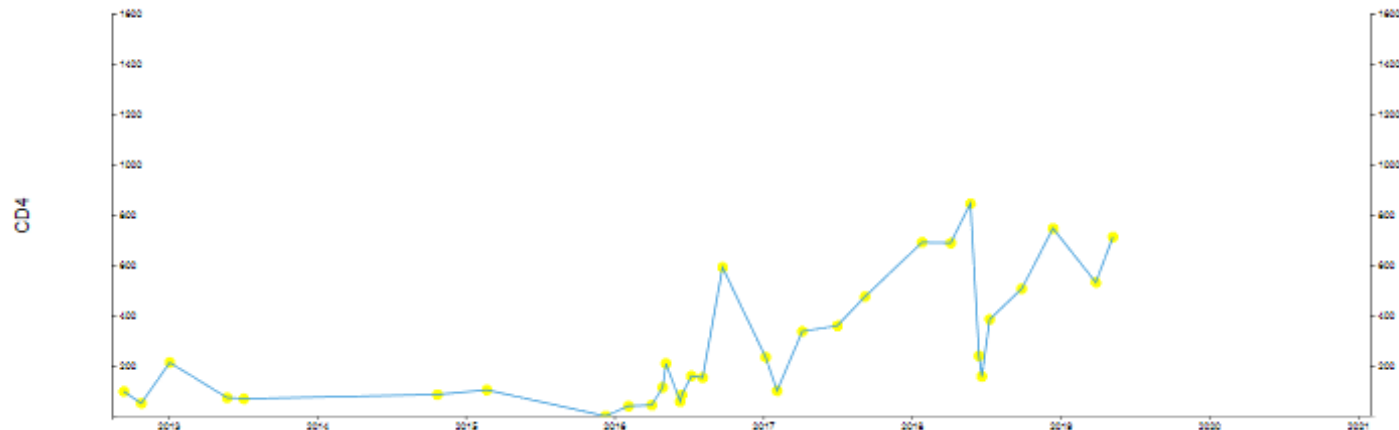
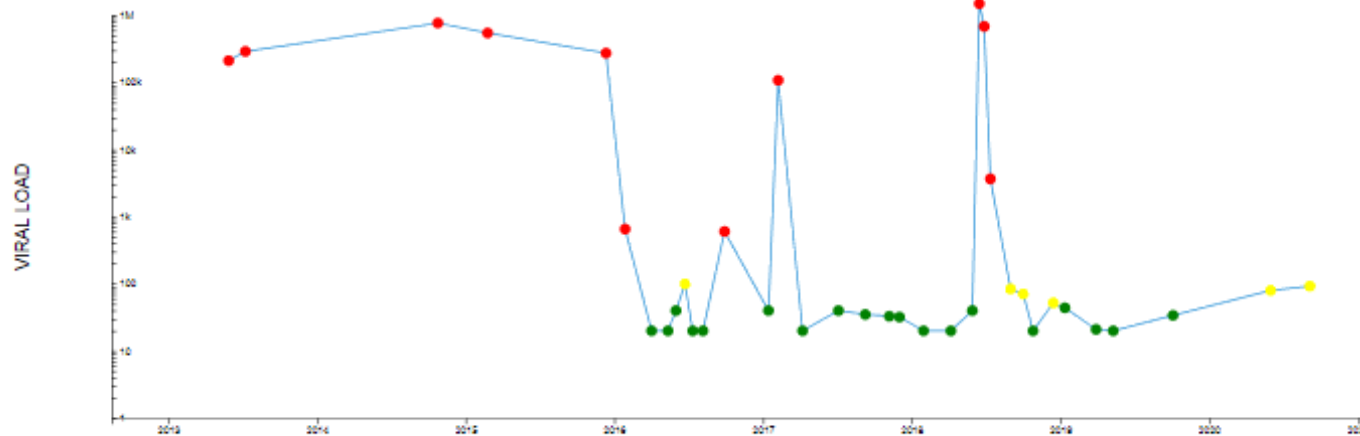
Imperial College Healthcare



NHS Trust



Mid 2018: Switches to Ataz/r, TDF, FTC





Careful consideration when responding to new data: dolutegravir and pregnancy

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² Imperial College, London, UK

Abstract

This case highlights the current complexities of managing women in the early stages of pregnancy presenting on dolutegravir-based regimens. When responding to new data, there is an important decision to be made, between the potential, uncertain risk of teratogenicity against the potential increased risk of *in utero* vertical transmission of HIV-1.

Keywords: dolutegravir, pregnancy, treatment switch

Introduction

A young adult taking Trimeq, a fixed dose combination of dolutegravir, lamivudine and abacavir attended HIV services with an unplanned 5-week (by dates) pregnancy. On that day, her CD4 cell count was 848 cells/mm³, CD4:8 ratio 0.5 and HIV viral load (VL) <20 copies/ml.

HIV infection was first diagnosed at age 6 and she had a history of longstanding poor adherence to antiretroviral therapy (ART) presenting in 2016 with disseminated mycobacterium avium intracellulare with a nadir CD4 cell count of 5 cells/mm³. Despite antimicrobial therapy and excellent immune reconstitution on fully suppressive dolutegravir-based ART, recovery was complicated by bilateral hearing loss requiring augmentation.

Five days previously (18th May 2018) increased rates of neural tube defects (NTD) in infants conceived on dolutegravir were reported in the Botswana cohort: 4/426 infants. This was a rate of any NTD of 0.9% compared to an expected rate of 0.1% [1]. In response, the European Medicines Authority recommended 'If pregnancy is confirmed in the first trimester while a woman is taking dolutegravir, switch to an alternative treatment unless there is no suitable alternative' [2].

Outcome

Following discussions with the patient and her supporter, she switched to darunavir/ritonavir and abacavir co-formulated with lamivudine and additional folic acid. Concerns with adherence and previous resistance mutations impacted on non-nucleoside reverse transcriptase inhibitors favouring a boosted protease inhibitor regimen over raltegravir or efavirenz-based ART. At follow up, 21 days after the switch, she reported difficulties with adherence,

nausea and tiredness. Despite 16 months with suppressed viraemia on Trimeq, 21 days following ART switch her HIV VL was 1,505,162 copies RNA/ml and CD4 cell count had fallen to 242 cells/mm³, CD4:8 ratio 0.2. A week later she was switched back to Trimeq at 10 weeks' gestation. Her CD4 cell count was now 161 cells/mm³ and prophylaxis against *Pneumocystis jirovecii* pneumonia was re-instigated. She continues under fortnightly follow up until viral suppression is regained.

Discussion

This case highlights the current complexities of managing women in the early stages of pregnancy presenting on dolutegravir-based regimens, particularly in those with a history of poor adherence in whom outcomes of treatment switches, that increase both pill burden and potential toxicity, are of concern. By 5 weeks' gestation, the fetal neural tube is already closed raising the question of benefit of switching after this time. When responding to new data, there is an important decision to be made, between the potential, uncertain risk of teratogenicity against the potential increased risk of *in utero* vertical transmission of HIV-1. The challenge now is to achieve viral re-suppression before delivery to prevent peripartum transmission, complex for a young woman who has struggled with adherence and now has the added anxiety that ART can harm her unborn child. In retrospect perhaps there was no 'suitable alternative'.

References

1. World Health Organization. Statement on DTG. Potential safety issue affecting women living with HIV using dolutegravir at the time of conception. 18 May 2018. Available at: www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf (accessed June 2018).
2. European Medicines Agency. New study suggests risk of birth defects in babies born to women on HIV medicine dolutegravir. Press release 18 May 2018. Available at: www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/05/news_detail_002956.jsp&mid=WC0b01ac258004d5c1 (accessed June 2018).

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Email: caroline.foster5@nhs.net

**A MISTAKE
IS ONLY A
MISTAKE
WHEN YOU
DON'T LEARN
FROM IT.
OTHERWISE
IT IS A
LESSON.**

PictureQuotes.com

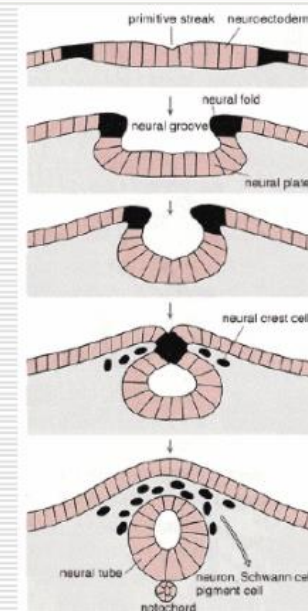


Hindsight:

- Never tolerated a protease inhibitor based regimen in past
- Uninfected partner and infant at potential risk of infection if viral rebound
- Neural tube defects – possible increased risk on dolutegravir but the neural tube closes by 26 days of pregnancy

Normal embryological development

- ❑ Neural plate development -18th day
- ❑ Cranial closure 24th day (upper spine)
- ❑ Caudal closure 26th day (lower spine)





22 year old young woman living with PHIV requesting injectable ART

- CD4 70, VL 748,000
- Long term poor adherence to ART
- 2015 CNS venous thrombosis (s/c LMWH)
- Learning Disability
- Obesity

Novel Adherence Interventions in Perinatally Acquired HIV: PEG Insertion and Pill Glide. Zombori et al. Clin Drug Investig. 2020 Aug;40(8):765-772.



ART Treatment

Date	ART	CD4/VL
8/97-10/97	NVP D4T DDI	
10/97-12/02	D4T DDI	
12/02-09/03	EFV ABC 3TC	
09/03-10/11	Off ART	CD4 fell to 195
10/11-1/12	DRV/r TDF/FTC	
1/12-4/13	KAL liquid TDF/FTC	VL suppressed for 9/12
4/13-2014	DRV/r TDF/FTC	Last VL <50 march 2013
2015-2018	DRV/r TDF/FTC	VL<50 then stopped
4/18-2/19	DTG + F/TAF	VL 24 then stopped

Drug Resistance Interpretation: RT

NRTI Resistance Mutations:	None
NNRTI Resistance Mutations:	K103N
Other Mutations:	None

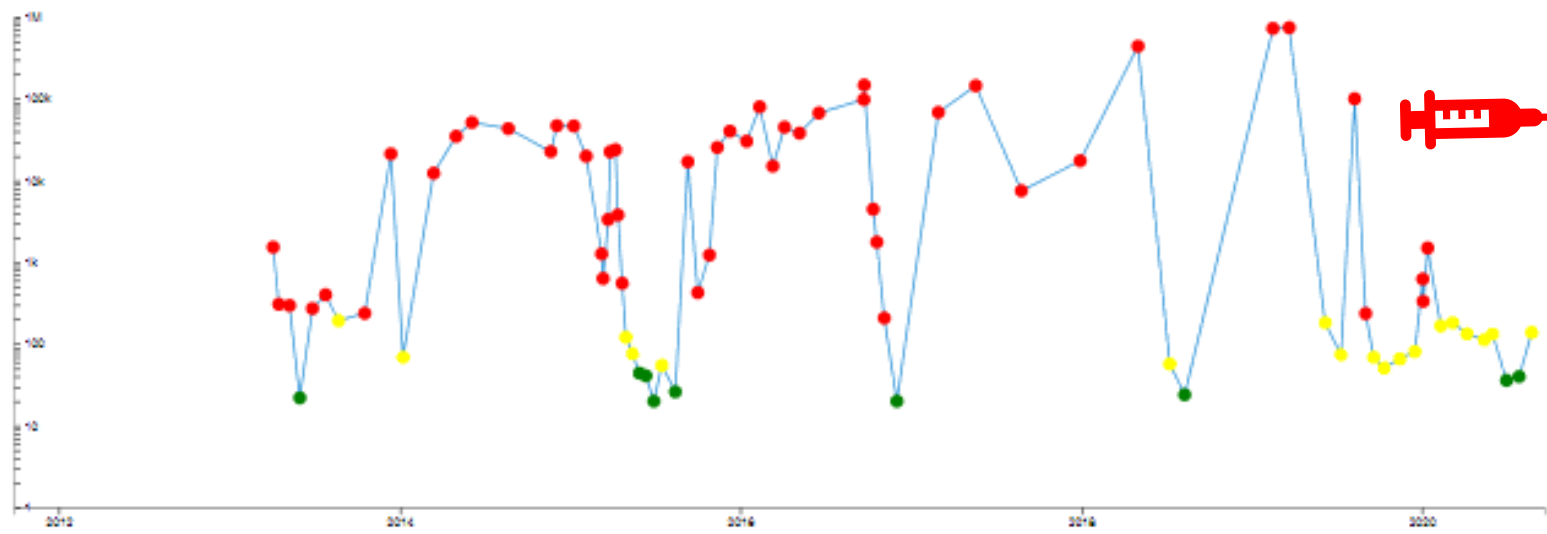
Non-Nucleoside RTI

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

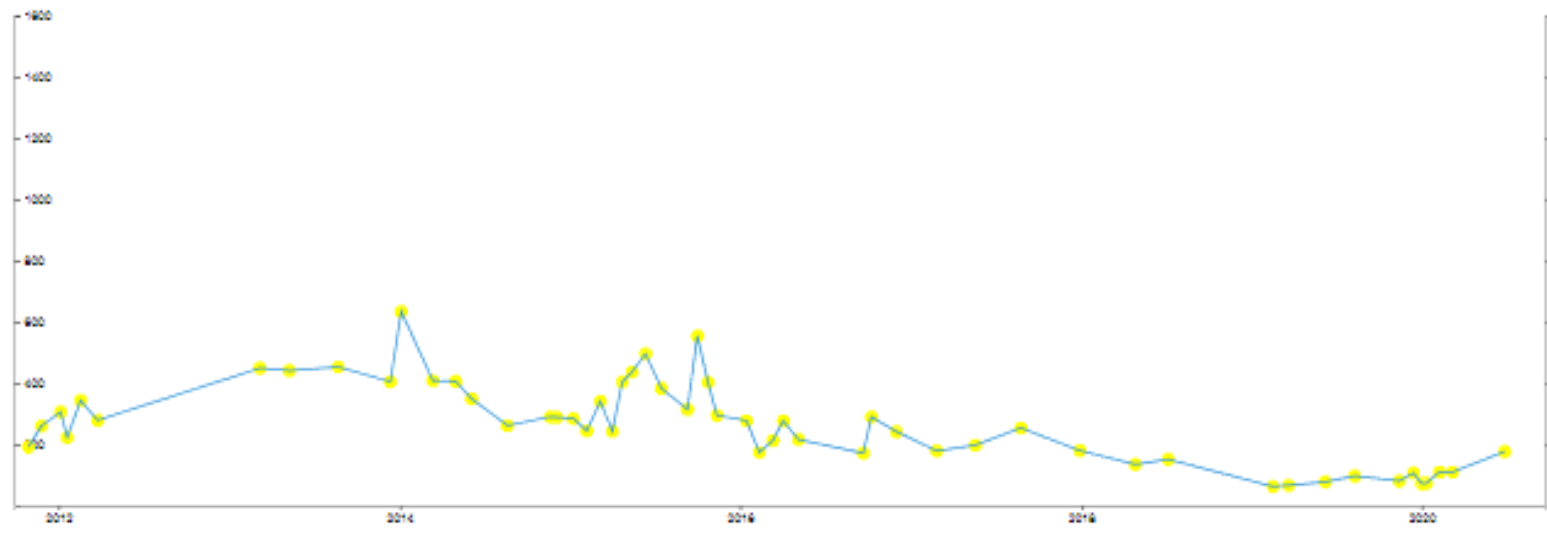
2012 2013 2014 2015 2016 2017 2018 2019 2020



VIRAL LOAD



CD4

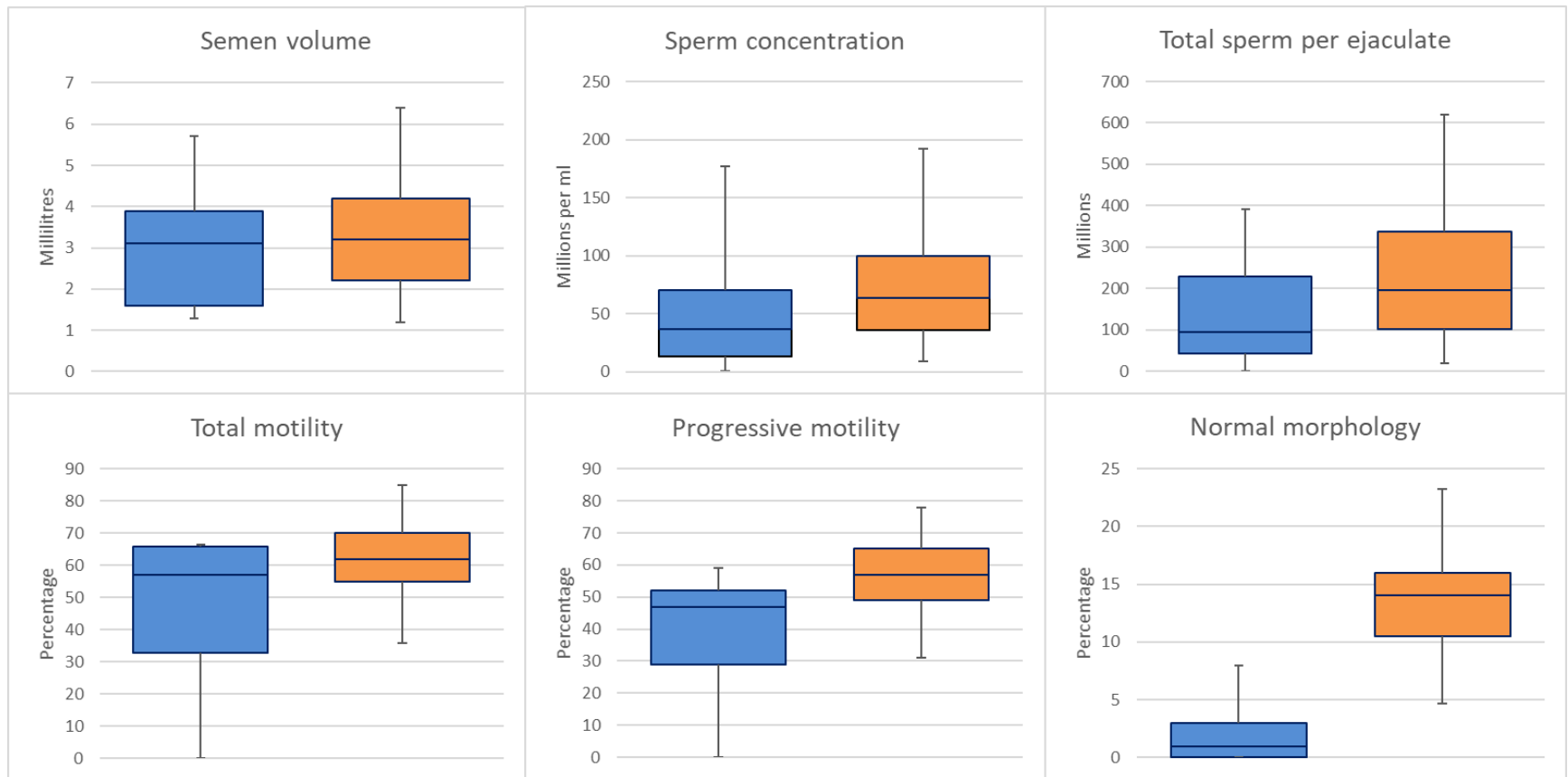




Fertility evaluation in adults with perinatally acquired HIV-1 infection: a cross-sectional observational study *Pasvol et al AIDS in press 2020*



Fig 2. Box and whisker plots of seminal fluid analysis data

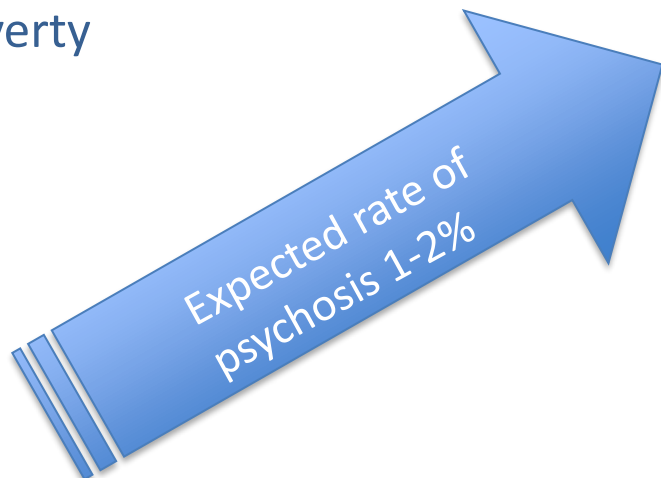


Mental Health

AALPHI Perinatal UK cohort: similar to matched HUE siblings, but higher than the general population *Le Provost AIDS Care 2018*

UK Risk factors for adverse Adolescent Mental Health

- Black ethnicity
- Migrant population
- Parental unemployment
- Looked after child
- Poverty



21% anxiety/depression
4.5% suicide/self harm
4% alcohol/drug dependency

7.5% psychotic episode
median 21 yrs (r14-26)
66% suppressive ART

Malik 2002 in press

Prescribing ART is the easy part

Late HIV/ART toxicity

Neuropsychiatric

3rd generation

Malignancy

Renal

Bone

CVS

OIs







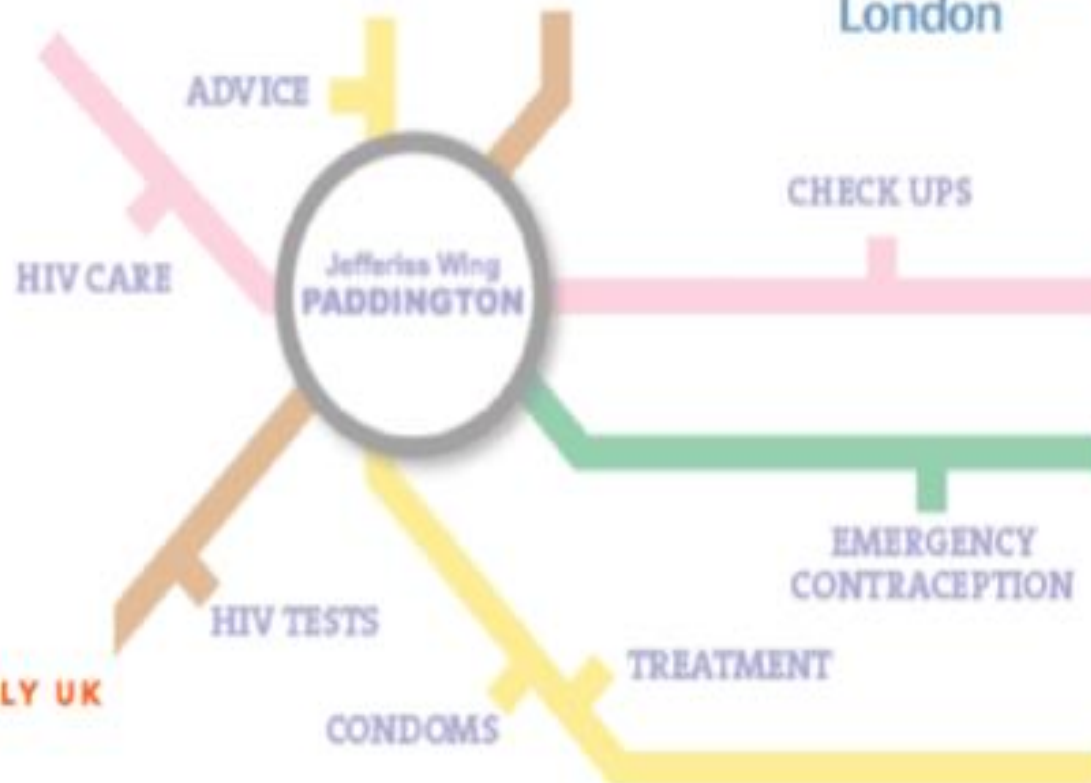
Children adolescents, young adults and not so young adults of the 900 and Family Clinics



Imperial College Healthcare NHS Trust



Imperial College London



900 @ JW

S Fidler

S Ayers

G Frize

N Kirkhope

N Mackie

T Pasvol

A Al-Dujaili

Family Clinic

EGH Lyall

G Tudor-Williams

P Seery

S Raghunanan

N Tickner

F Mathias

T Popoola

S Meah