

Ageing of adult lifetime survivors with perinatal HIV

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ASK A QUESTION HERE



Aging with perinatal HIV

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Disclosures

- Speaker fees, educational meeting support: Gilead Sciences, ViiV
- Nil in relation to this presentation

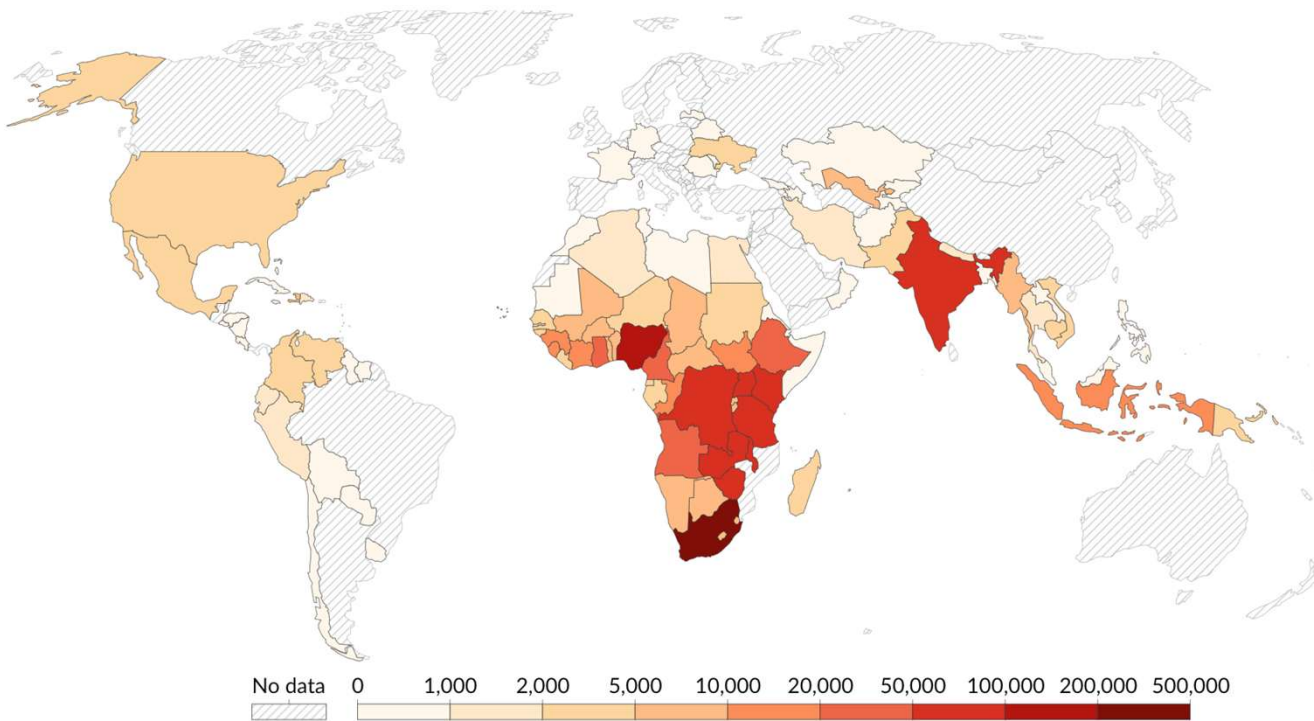
Outline

1	Epidemiology and characteristics of adults with perinatal HIV
2	Emerging virological outcomes
3	Emerging clinical outcomes
4	Data gaps and the way forward

1

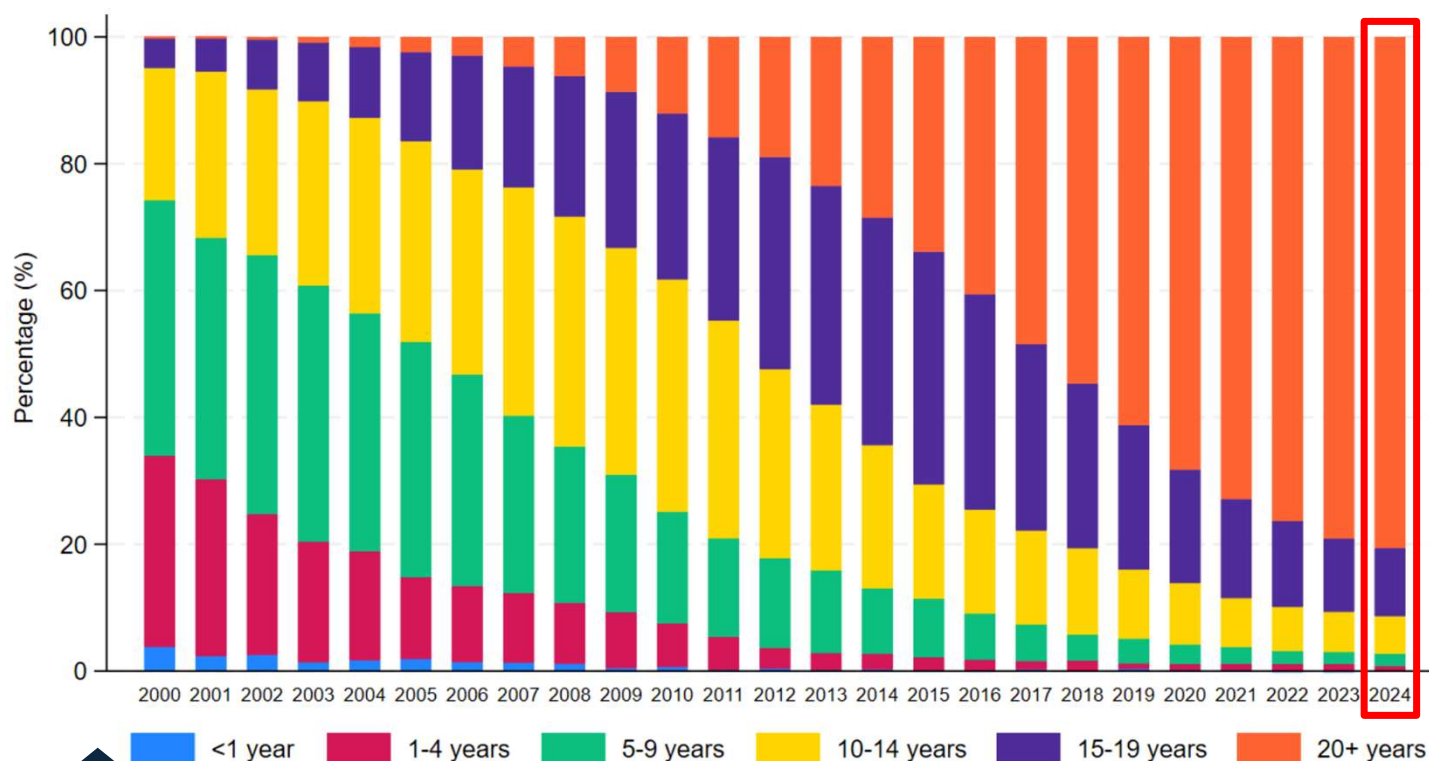
**Epidemiology and characteristics of
adults with perinatally acquired HIV**

Epidemiology of perinatally acquired HIV



- ~11 million born with HIV since 1990
 - 90% in Africa
- 660,000 adults with perinatal HIV globally in 2023 (20–24y)
- Unknown number aged >24 yrs
- 120,000 new diagnoses 0-14 yrs 2024

Changing age distribution of people in England with HIV diagnosed in childhood (n=1,569), 2000-2024



Two important points:

1. >80% over 20 years

- Some >40 years¹

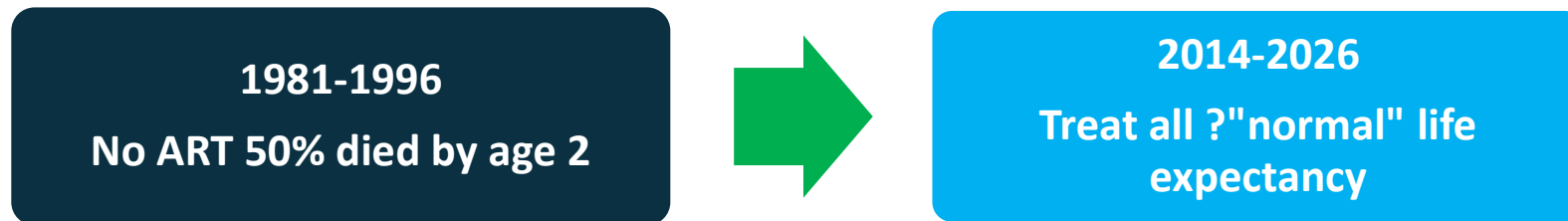
2. Potentially two cohorts:

- Biological differences
 - Age cohort
 - Timing of ART

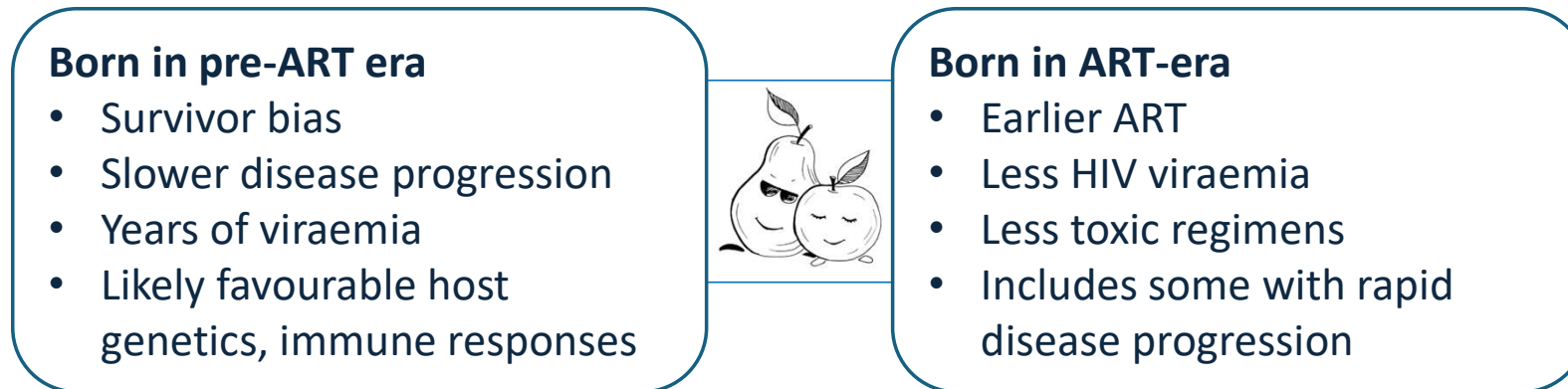
Paediatric ART
Late 1990s

Two cohorts with perinatally acquired HIV

UK, Europe and US earlier access to paediatric ART (late 1990s)



Potentially **two cohorts**



2

Emerging virological outcomes

Viral suppression and drug resistance

Lower rates of viral suppression in adults with perinatally acquired HIV (44-90% globally¹⁻⁴)

U.K. data – Cumulative HIV drug resistance⁴

- **n=280**; median age 26 (IQR 21, 30) years
- 99% on ART, 90% VL <200 c/mL
 - Median years on ART 17 (IQR 11, 22)
 - 78% exposed to NNRTIs
- **43% any acquired resistance**
 - 25% ≥ dual class
 - 4.6% ≥ triple class; 85% aged ≥ 25 years
- Factors associated with DRMs
 - Length of ART (p=0.007)
 - Prior NRTI mono/dual therapy (p=0.008)

DRM by drug class	Age group (years), n (%)	
	0-24	25+
NRTI	22 (20)	56 (34)
NNRTI	34 (30)	70 (42)
PI	2 (2)	13 (8)
INSTI	2 (2)	1 (1)
Multi-class (2+)	16 (14)	53 (32)

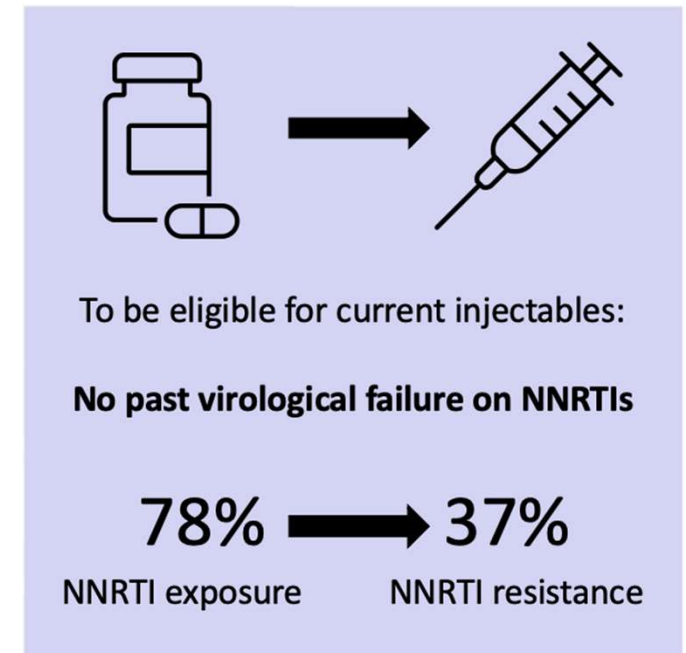
Abbreviations: DRM (drug resistance mutations)

Data gap

**What are the optimal therapeutic strategies
in adults with perinatally acquired HIV?**

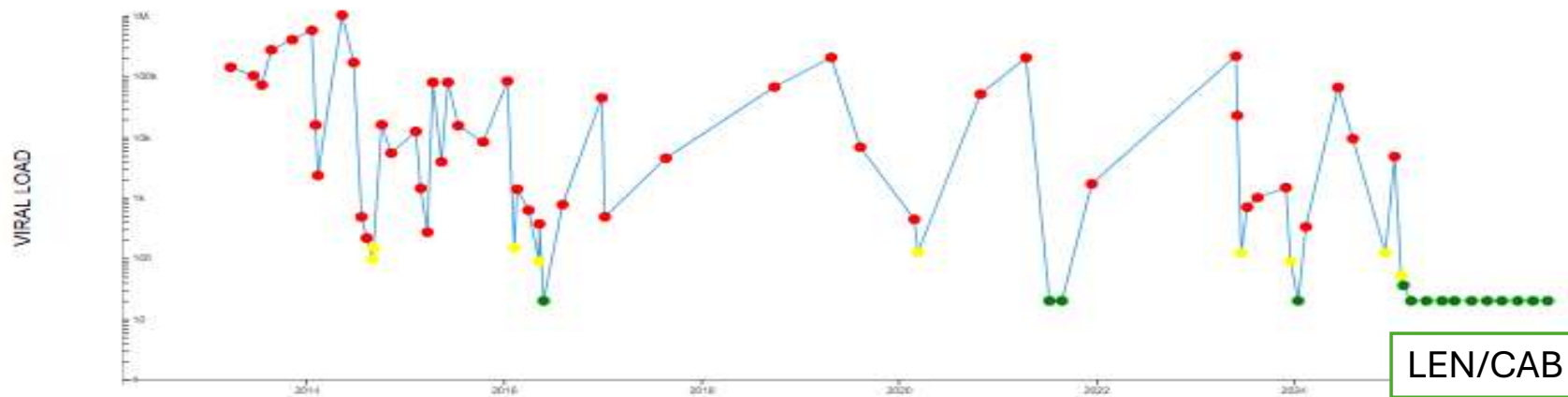
Long-acting injectables and perinatal HIV

- NNRTIs mainstay of paediatric ART prior to dolutegravir (e.g. UK, Southern Africa)
- Extensive prior NNRTI exposure renders long-acting (LA) CAB/RIL unsuitable for many
- Future bright → new LA agents in development
 - 3rd generation integrase inhibitors
 - Novel capsid inhibitors
 - Broadly neutralising antibodies



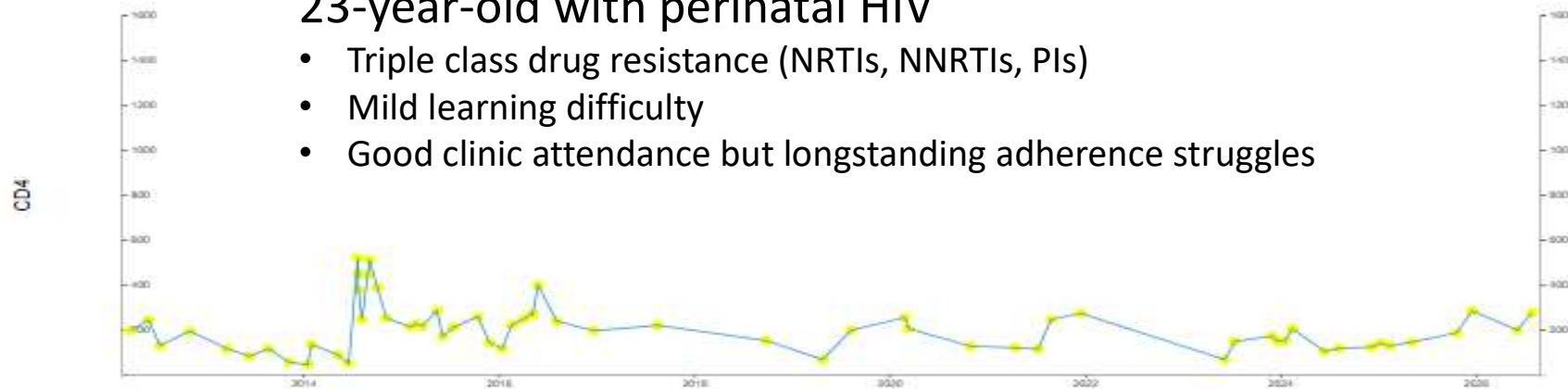
Glenn. AIDS. 2025.

Case 1. Lenacapvir (LEN) + Cabotegravir (CAB).



23-year-old with perinatal HIV

- Triple class drug resistance (NRTIs, NNRTIs, PIs)
- Mild learning difficulty
- Good clinic attendance but longstanding adherence struggles



Abbreviations: NRTI (nucleoside reverse transcriptase inhibitors), NNRTI (non-nucleoside reverse transcriptase inhibitors), PI (protease inhibitors).

3

Emerging clinical outcomes

UK Hospitalisation rates

- U.K. admission incidence in young people with perinatally acquired HIV¹:
 - 3.0 (CI 1.4-5.8) per 100 person years 10-19 years
 - 13.4 (CI 10.0-17.6) per 100 person years 20-35 years*

***Rates for young adults with perinatally acquired HIV 4x higher than UK adults with HIV**

- 89% admissions HIV-related and associated with disease severity:
 - CD4 <200 cells/uL – incidence rate ratio 4.0 (CI 1.8-8.8)
 - Prior AIDS diagnosis – incidence rate ratio 2.9 (CI 1.6-5.3)

UK all-cause mortality

- Mortality 10x age-matched UK general population¹
- HIV-associated opportunistic infections and malignancies
- But ?changing clinical picture, also non-AIDS related mortality

2023
Male age 30 years
CD4 490, VL <20
Post-mortem: PE/DVT



2023
Female age 24 years
CD4 408, VL 80
Post-mortem: ?arrythmia

Emerging adult morbidity (despite viral suppression)



Cardiometabolic

Subclinical cardiac and vascular changes

Cardiomyopathy

Cardiac fibrosis and inflammation

Higher rates of hypertension/diabetes

Adverse bone health



Respiratory

Higher rates of chronic lung disease

- Clinical or radiological

U.K. 47% abnormal chest x-ray

- 8% bronchiectasis or bronchiolitis

U.S. higher rates fixed airways obstruction



Sexual and reproductive health

Higher rates of HPV persistence

Reduced fertility

Third generation outcomes:

- Preterm delivery
- Low birth weight/S-G-A
- HIV exposed uninfected infants?



Neurocognitive and mental health

Legacy effects of advanced HIV on cognition

Higher rates of mental health disorders:

- Anxiety
- Depression
- Psychosis
- PTSD



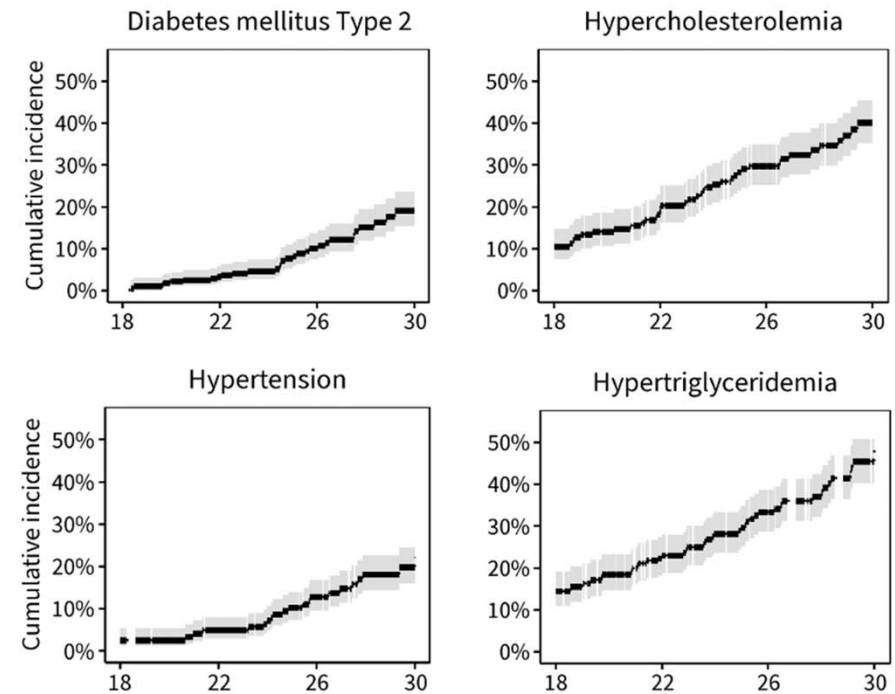
Metabolic outcomes

USA NA-ACCORD cohort (n=357, aged 18-30 years), estimated cumulative incidence by age 30¹:

- 19% type 2 diabetes
- 40% hypercholesterolaemia
- 50% hypertriglyceridaemia
- 22% hypertension

Incidence rates higher across all outcomes, when compared to age-similar general US population

- ~3-6x diabetes
- ~2x hypercholesterolaemia
- ~2x hypertension





Metabolic outcomes

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HIV-related risk factors

- 30 years of HIV exposure
- Chronic immune activation
- ART – protease inhibitors

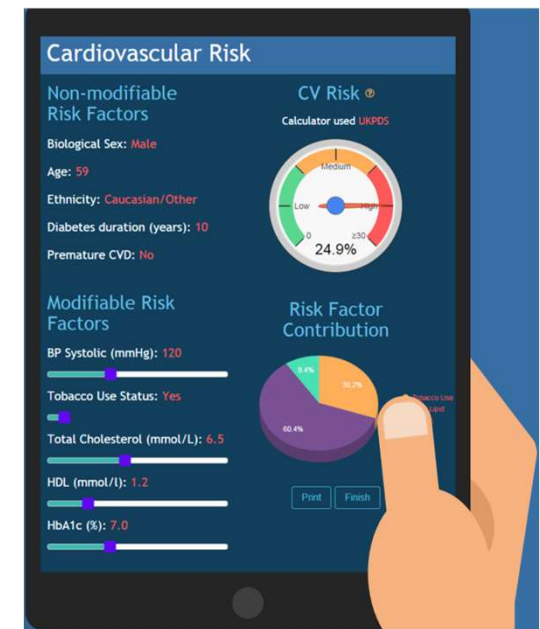
Non-HIV-related risk factors

- Diet/obesity
- Smoking
- Lack of exercise
- Ethnicity

Cardiovascular outcomes



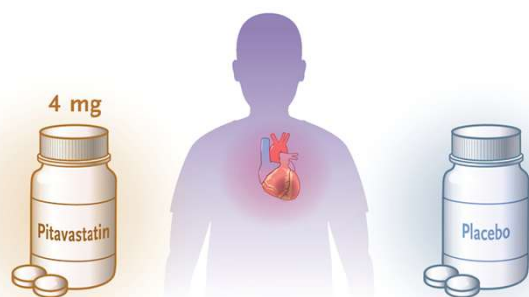
- Adults with perinatal HIV at elevated risk of cardiovascular disease
- Subclinical abnormalities in cardiovascular structure/function¹
 - Correlation with coronary plaque formation / clinical outcomes unclear
- Pathological Determinants of Atherosclerosis in Youth (PDAY) score
 - Validated cardiovascular risk assessment tool for those <40 yrs
 - Estimates risk of subclinical lesions based on traditional risk factors
- U.K. cohort – elevated PDAY score 57%
 - n=225, aged 18-40 yrs²
 - Associated factors: HIV viraemia, advanced HIV, protease inhibitor exposure



Cardiovascular disease



Randomized Trial to Prevent Vascular Events in HIV



BHIVA rapid guidance on the use of statins for primary prevention of cardiovascular disease in people living with HIV v2

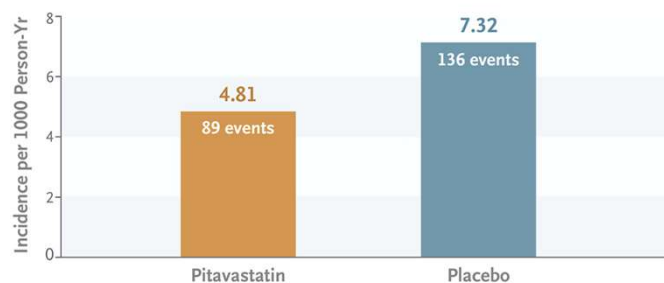
22 March 2024

Review date: 22 March 2025

We recommend that all people living with HIV aged 40 years or older should be offered a statin for primary prevention of CVD irrespective of lipid profile or estimated CVD risk (Grade 1B).

Major Adverse Cardiovascular Events

HR, 0.65 (95% CI, 0.48–0.90); P=0.002



Insufficient data to inform interventions in those with perinatal HIV <40 years

Is aging about age?

35 y/o male, John

Diagnosed with HIV aged 4 months
Previous pneumocystis pneumonia
Started ART aged 8
Behavioural difficulties as child
Psychosis aged 20
Dual class HIV drug-resistance

Years with HIV: 34

Years on ART: 28

Risk prevention strategies: ??

46 y/o male, Mark

Diagnosed with HIV aged 40
No prior AIDS-illnesses
Started ART straight away
Otherwise well
On statin for CVD risk prevention
No documented drug resistance

Years with HIV: 6

Years on ART: 6

Risk prevention strategies: statin

Early, proactive metabolic and cardiovascular screening needed



Renal outcomes

USA NA-ACCORD cohort (n=357, aged 18-30), estimated cumulative incidence by age 30¹:

- 4% chronic kidney disease (CKD) (eGFR <60ml/min/1.73m² for >3 months)
- 25% abnormal renal function (eGFR <90ml/min/1.73m² for >3 months)
- Incidence rates increase with age

Risk factors¹⁻⁴:

- Increasing age
- Hypertension
- Hyperglycaemia
- Sickle cell
- Black ethnicity
- Years of HIV viraemia
- CD8 activation
- ART - TDF

Sub-Saharan Africa: a pooled CKD prevalence of ~12% (limitation=heterogeneity of definitions)

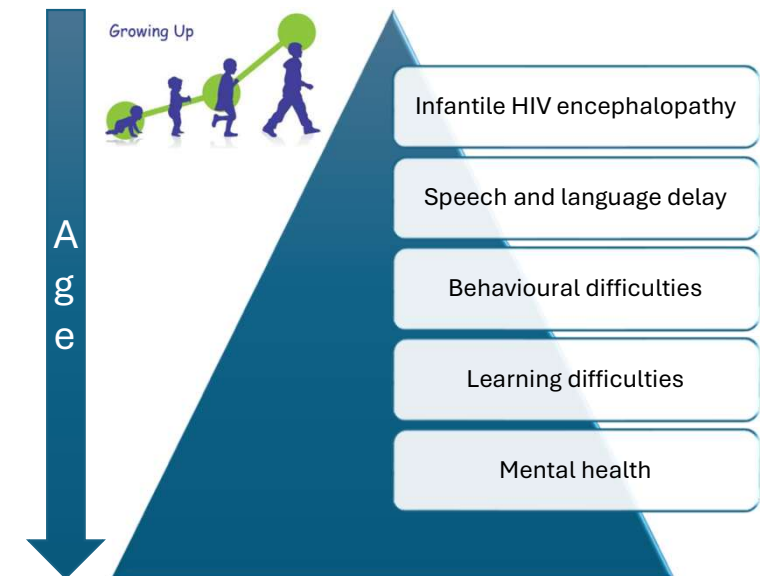
Neurocognitive and mental health outcomes



- Legacy effects of advanced HIV on a developing brain may impact on cognitive function¹
- Higher rates of mental health disorders

Psychosis U.K. multi-centre study²

- 377 perinatal HIV age 24 (IQR 20-27) years
- 82% black ethnicity, 62% born outside UK
- Psychosis 7.2% vs 0.5-1% in general population³
- 68% on suppressive ART; median CD4 650
- Associated factors: prior AIDS diagnosis, parental bereavement, cannabis use, family history mental health



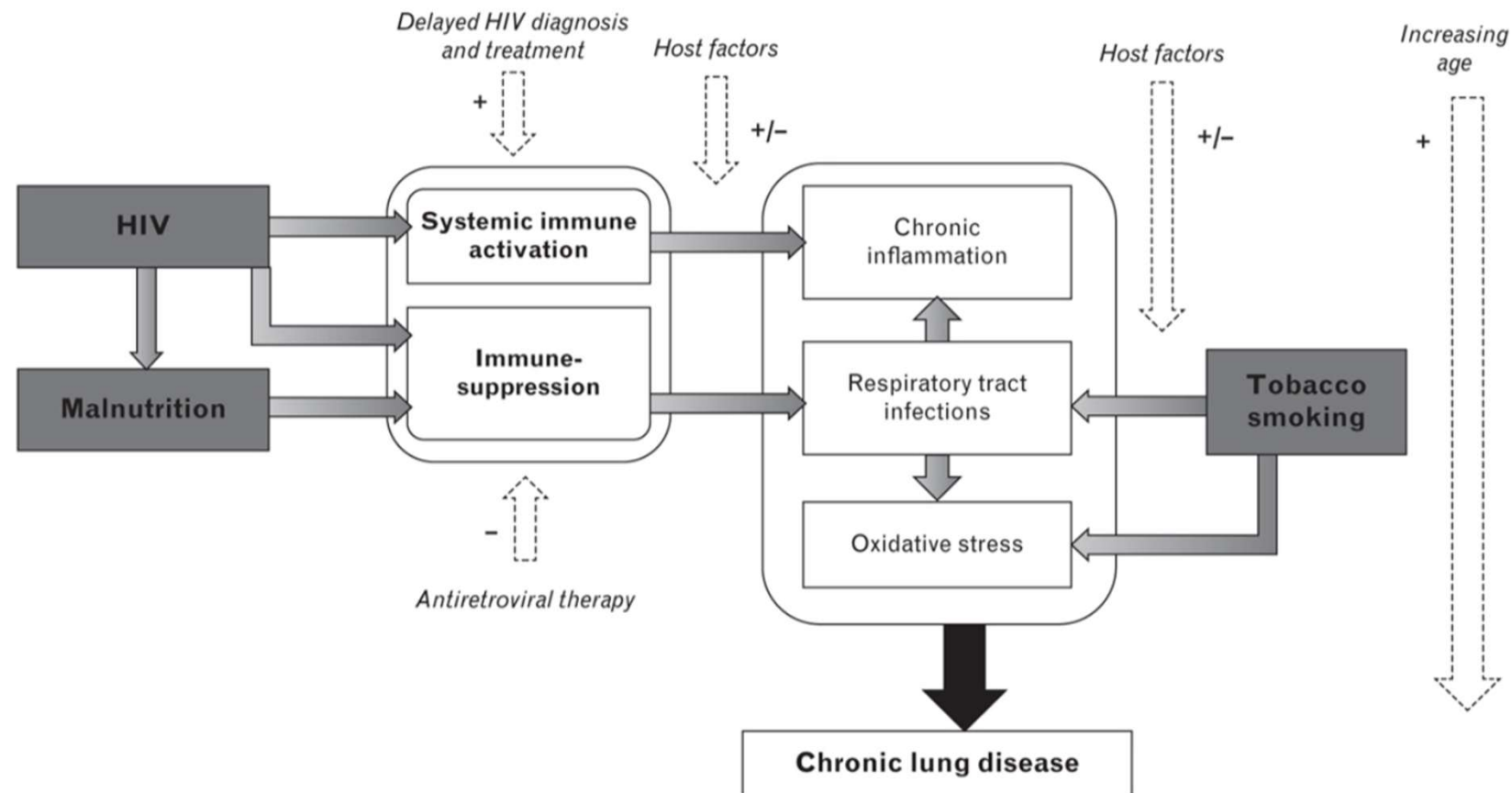
Respiratory outcomes



Chronic lung disease – important long-term complication

- Most data children/adolescents with perinatally acquired HIV, **limited data in adults**
- Bronchiectasis/obliterative bronchiolitis most common¹
 - UK cohort, n=98, age 17 (IQR 14 – 21) years
 - Abnormal chest x-ray 47%
 - Bronchiectasis/obliterative bronchiolitis 8%
- Greatest burden LMIC, lower rates in HIC²
 - Relevance for UK cohorts - high proportion migrants from other countries

Respiratory outcomes



The next (third) generation...

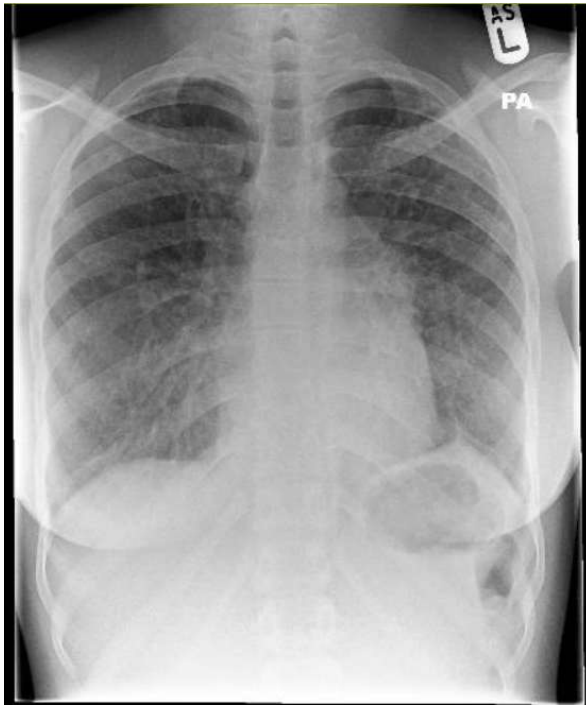


- UK = very low rates of vertical HIV transmission
- Increasing number of children exposed to HIV during pregnancy, who do not acquire HIV themselves
- Subtle differences in early growth and development in those exposed to perinatal vs non-perinatal HIV, associated with being small for gestational age and maternal viraemia¹
- Does lifelong HIV/ART exposure influence outcomes of next generation?
- Need global disaggregation of data by route of transmission

-
- The graph displays viral load on a logarithmic y-axis (ranging from 1 to 100,000) against time on the x-axis (from 2016 to 2021). The data points are connected by a blue line. Most of the time, the viral load is low, represented by green dots at approximately 10-20 units. There are three prominent peaks, each marked with a red dot, indicating high viral load. The first peak occurs around late 2017, reaching approximately 15,000. The second peak occurs around late 2018, reaching approximately 10,000. The third peak occurs around late 2019, reaching approximately 1,000. The viral load returns to low levels after each peak.

Abbreviations: INSTI (integrase strand transfer inhibitor), VZV (varicella zoster virus)

Age 21 – progressive fibrotic interstitial lung disease



2012 – Age 21



2024 – Age 33

? Cause – Atypical sarcoid-like VS Lymphoid Interstitial Pneumonitis related to HIV.

3

Data gaps and the way forward

Data Gaps

1. Do outcomes for those in their 30s/40s reflect the younger generation?
2. Does very early infant ART prevent comorbidities?
3. Will subclinical findings translate into clinical disease?
4. Interventions: ?Early statins, antihypertensives, immunomodulators

Most guidelines remain age-based – ?missed opportunities for screening



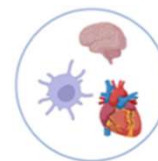
Social
determinants
of health



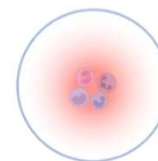
Traditional risk factors



Health behaviours



HIV and ART
exposure during
development



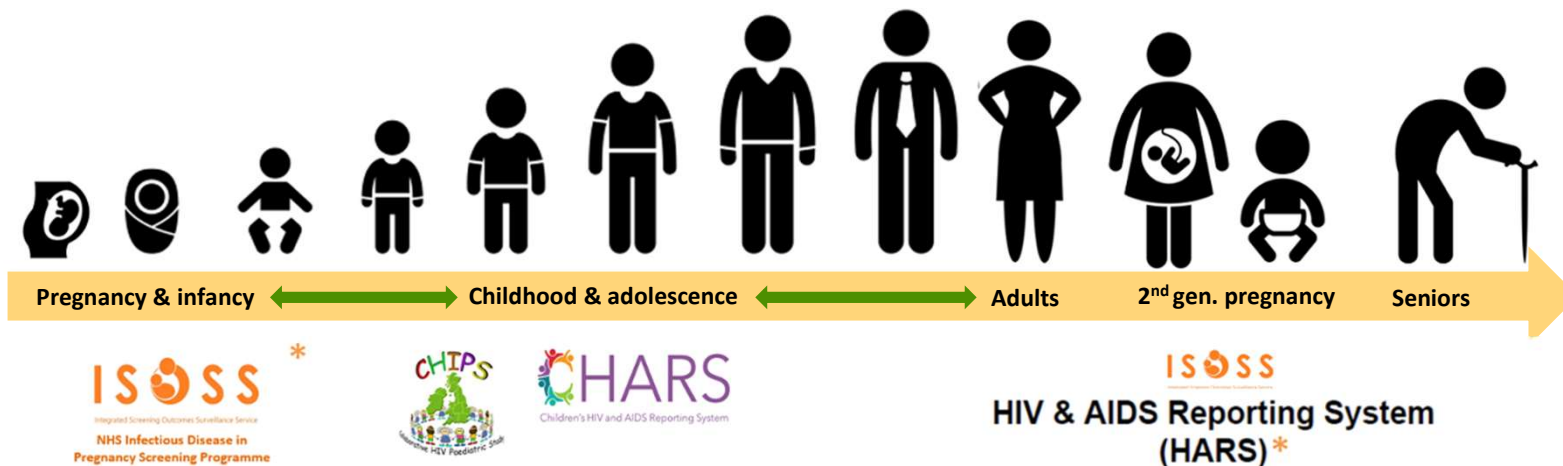
Chronic immune
activation and
inflammation



Longer ART
Exposed to older,
toxic regimens

The way forward...

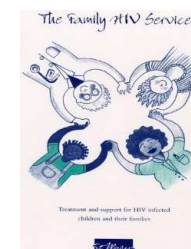
1. Link HIV datasets to understand how health develops with age
2. Early diagnosis/treatment
3. Sustained viral suppression throughout development and adulthood



Summary

1	Global characteristics • People with perinatally acquired HIV aging • Two cohorts based on antiretroviral therapy exposure
2	Emerging virological outcomes • High rates of drug resistance
3	Emerging clinical outcomes: mortality and morbidity • Multisystem co-morbidities emerging
4	Data gaps • Understanding pathogenesis of co-morbidities • Preventing and managing co-morbidities

Children, adolescents, adults of the 900 & Family Clinics



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