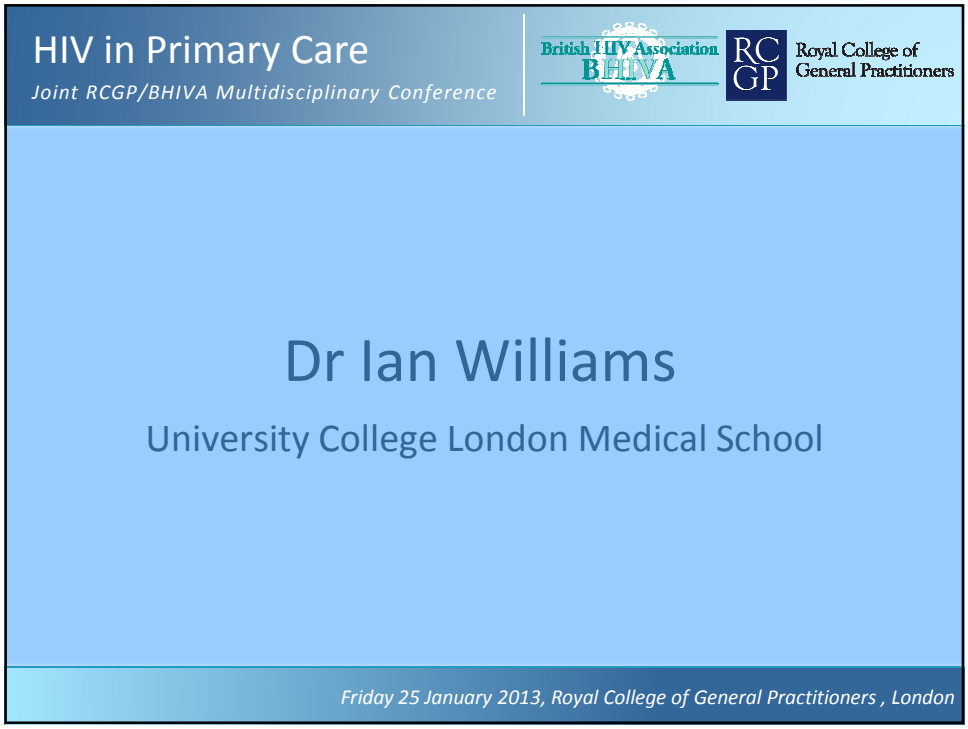
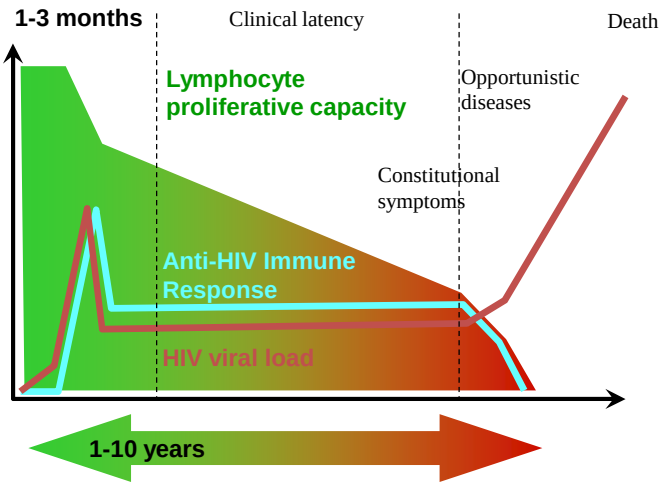


HIV Treatment and management

Dr Ian Williams
University College London

Natural history of HIV Infection



HIV infection is a chronic medical condition requiring and integrated care model

Main management issues

Managing HIV infection

- Assessment risk of clinical disease progression
- Initiation of anti-retroviral therapy
- Monitoring response to therapy (efficacy and safety)
- Managing treatment failure and HIV drug resistance
- Treatment of complications of HIV disease
- Screening and management of non-AIDS co-morbidities (infectious and non-infectious)

Main Management issues

Psychological

- Adjustment reactions
- Disclosure / Stigma
- Depression/anxiety
- ART non-adherence and health care beliefs
- HIV and ageing
- Neurocognitive impairment

Prevention: reduce onward transmission

- Partner notification
- Assess risk behaviour
- Prevent mother to child to transmission
- Early initiation of ART

Main management issues

Sexual and reproductive health

- **Screen and treatment of STIs**
- **Risk behaviour:**
- **Women's health:**
  - **Contraception**
  - **Pregnancy planning and management**
  - **Cervical screening**
- **Sexual dysfunction**

Social and welfare support

- **Liaise with welfare/ Housing services**

Promotion of self management

- **patient education and advocacy**

Monitoring of HIV infection

Markers of HIV disease:

- T Helper lymphocyte count (CD4): Marker of degree of Immune deficiency
- Plasma HIV RNA level (Viral load): Measurement of level of viral activity
- symptoms: consequence of Immune deficiency

Lymphocyte sub-set profile

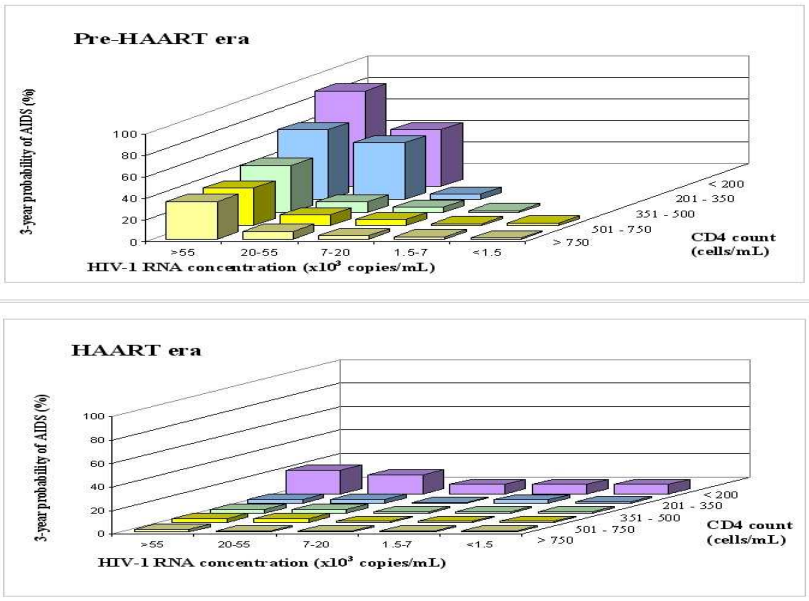
	Result	Normal range
White cell count	3.75 x 10^9/L	3.0-10.0
Lymphocyte count	0.97 x 10^9/L	1.2 -3.6
CD4 absolute count	0.03 x 10^9/L	0.44 -1.47
CD4 percentage	2.8%	31 -64
CD8 absolute count	1.25 x 10^9/L	0.29-1.05
CD4/CD8 ratio	0.02	0.54-2.97

Clinical progression

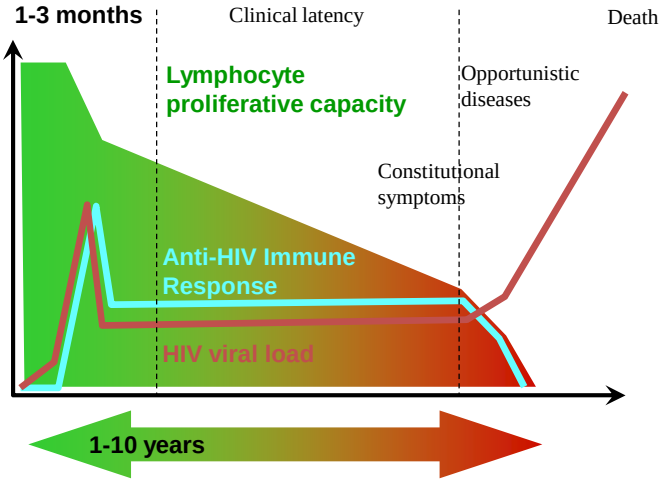
Viral load Copies/ml	CD4 cell count x10^6/L					
	50	100	200	300	400	500
3,000	10.7	5.9	2.5	1.3	0.7	0.5
10,000	15.1	8.5	3.6	1.9	1.1	0.7
30,000	20.6	11.7	5.1	2.6	1.5	0.9
100,000	28.4	16.5	7.3	3.8	2.2	1.3
300,000	37.4	22.4	10.1	5.3	3.1	1.9

Predicted 6 month risk of AIDS
Separate tables for different age groups
Data derived from multiple sources in cluding Cascade and ART collaboration cohorts

Figure A: Prognosis According to CD4 Cell Count and Viral Load in the Pre-HAART and HAART Eras



When to start ART



BHIVA 2012 When to start: Chronic infection

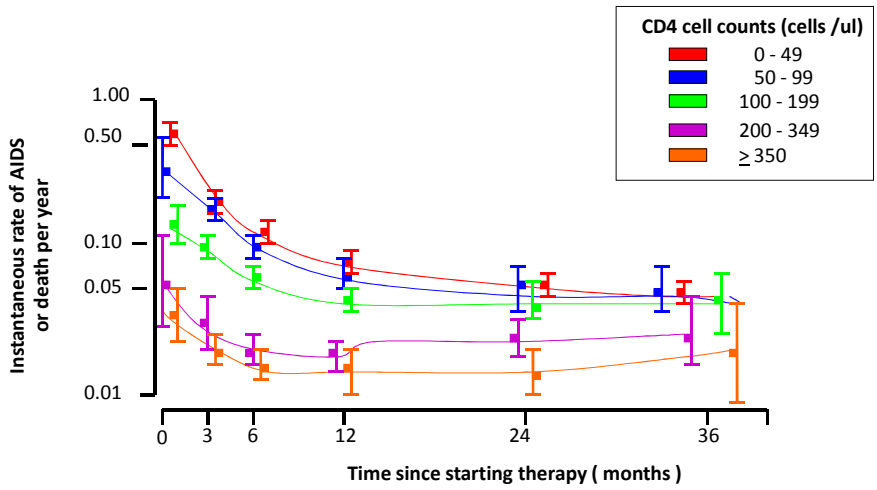
4.1.1 Recommendations

•We recommend patients with chronic infection start ART if the CD4 count is ≤350 cells/µL [1A]: it is important not to delay treatment initiation if the CD4 cell count is close to this threshold.

✓absolute risk of disease progression is significantly higher for a given CD4 count in older people , so consideration should be given to starting at higher CD4 counts in older persons.

✓Evidence from cohort studies suggest that the risk of disease progression is significantly higher once the CD4 count falls below 350 cells/µL, so it is important not to delay unnecessarily the initiation of ART if the CD4 count is close to this threshold.

ART Collaboration:



Egger M et al, Lancet 2002

BHIVA 2012When to start: Chronic infection

We recommend patients with the following conditions start ART:

- AIDS diagnosis (e.g. Kaposi's sarcoma) irrespective of CD4 cell count [1A];
- HIV-related co-morbidity including HIVAN [1C], ITP, [1C], symptomatic HIV-associated neurocognitive disorders irrespective of CD4 cell count [1C]
- Co-infection with hepatitis B virus if the CD4 count is ≤500 cells/μL [1B]
- Co-infection with hepatitis C virus if the CD4 count is ≤500 cells/μL [1C]
- Non-AIDS defining malignancies requiring immunosuppressive radiotherapy or chemotherapy [1C]

We suggest patients with the following conditions start ART:

- Co-infection with hepatitis B virus if the CD4 count is >500 cells/μL and treatment of hepatitis B is indicated [2B]

Treatment aims

- To prevent clinical disease progression as a consequence of immune reconstitution
- Reduce viral load to undetectable levels (<50 copies/ml) and maintain suppression over time.
- At low cost of drug toxicity
- Decrease risk of non-infectious co-morbidities
- Prevention of onward transmission

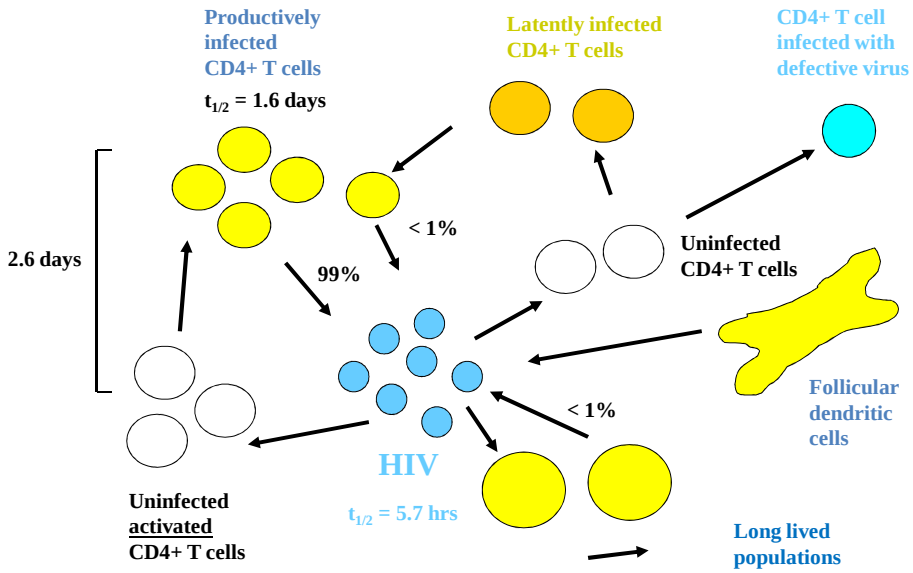
BHIVA 2012: What to start

	Preferred	Alternative
NRTI backbone	**Tenofovir and Emtricitabine**	**Abacavir[1] and Lamivudine[2]**
Third agent	**Atazanavir/rit Darunavir/rit Efavirenz Raltegravir**	**Lopinavir/rit Fosamprenavir/rit Nevirapine[3] Rilpivirine[2]**

1. Contraindicated if HLA B5701 positive
2. Recommended only if base line VL < 100, 000 copies /ml
3. Use according to CD4 count criteria Males <400, Females < 250

Antiretroviral therapy is life long

Dynamics of HIV infection in vivo

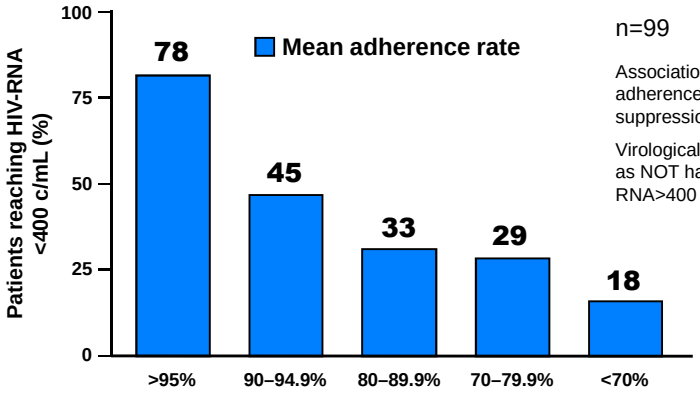


ART management

- Monitor response: HIV RNA, CD4 count
- Assess and support adherence
- Monitor for drug toxicity
- Manage drug-drug interactions
- Manage treatment failure:
  - drug resistance

High levels of adherence required… but not always attained

Relationship of adherence (measured by MEMS) to virologic success



n=99

Association between adherence and virological suppression $p<0.001$.

Virological success defined as NOT having an HIV RNA>400 at last visit.

Note: This study was only done with PIs

≥95% adherence is required for optimal virological suppression

Adapted from Paterson *DL et al., Ann Intern Med 2000*;**133**:21-30.

Cumulative risk of mutations from two / three classes: UK Resistance group

	2 years	4 years	6 years
Two classes	6%	14%	18%
Three classes	1%	2.5%	3.5%

Drug toxicity

Hypersensitivity:
- rash (stevens johnson
- hepatitis

Gastrointestinal:
- diarrhoea

Neuropsychiatric:
- sleep disturbance, vivid dreams
- mood disturbance

Renal:
- Tubulopathy/renal impairment
- Nephrolithiasis

Lipodystrophy:
Central adiposity, lipoatrophy

Drug toxicity

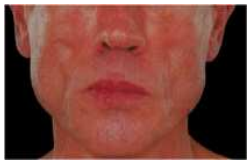
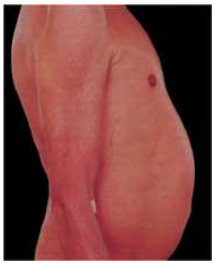
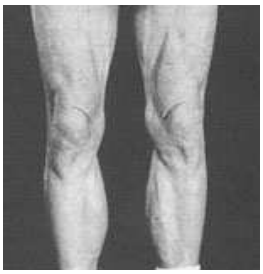
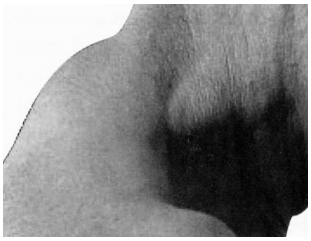
Metabolic:
- Hyperlipidaemia
- glucose intolerance

Liver:
- Acute hepatitis
- Hepatic steatosis

Bone:
- osteomalacia/ osteopaenia

Musculoskeletal:
- myalgia

HIV associated 'lipodystrophy syndrome'

Drug interactions

Drug class	Enzyme effect	Drug interaction
Protease inhibitors eg ritonavir	Inhibitor (cytochrome p450 enzymes)	↑↑ Drug levels (eg simvastatin, fluticasone, alfuzosin)
NNRTIs eg efavirenz	Inducer (cytochrome p450 enzymes)	↓/↓↓drug levels (eg: simvastatin, diltiazem, Methadone)

NRTIs and the integrase inhibitor have in general no clinically significant effect on the levels of other drugs

Drug interactions: ritonavir

Contra-indicated/not recommended	Caution: requires monitoring
Alfluzosin	Amiodipine
Amiodarone	Carbamazepine
Ergotamine	Citalopram
Flecainide	Clarithromycin (renal impairment)
Fluticasone	Diazepam
Midazolam	Diltiazem
Salmeterol	Estradiol OCP
Simvastatin	Methadone
	Sildenafil
	Sertraline
	Tamsulosin
	Triamcinolone

Liverpool University web site:

http://www.hiv-druginteractions.org/

Treatment as Prevention

Reduces Sexual transmission

- 93% reduction between discordant heterosexual couples in cohort studies and 1 RCT
- Reason for early initiation of therapy

Prevents mother to child transmission

- In UK <1%
- importance of universal testing in pregnant women
- Initiate ART in 2nd trimester
- avoid breast feeding