

The UK Collaborative HIV Cohort (UK CHIC) Study



Background

- Information on HIV infection in the UK comes from a variety of sources; these are often limited in scope
- Many clinical centres routinely collect information about patients with HIV infection as they attend for care
 - This provides an ideal opportunity to study HIV-infected individuals in their clinical setting
 - Can use existing infrastructure for data collection
 - Can include patients from a wide variety of clinics so that the cohort becomes more representative of individuals with HIV infection in the UK

Objectives of the UK CHIC Study

To collate routinely collected data from HIV-infected individuals attending some of the largest clinical centres in the UK since 1st January 1996 with the following aims:

- To describe the characteristics of patients with HIV under care
- To provide information on exposure to HAART and changes to the immunological and virological status of patients over time
- To monitor the frequency of AIDS and survival over time
- To use the information generated to describe the changing epidemic of HIV in the UK, and to generate models of disease progression in the HAART era

Participating centres

Clinical centres

Brighton and Sussex University Hospitals NHS Trust, Brighton
Barts and the London NHS Trust, London
Chelsea & Westminster NHS Trust, London
Mortimer Market Centre, RF&UC Medical School, London
Homerton University Hospital NHS Trust, London
Kings College Hospital, London
The Lothian University Hospitals NHS Trust, Edinburgh
The Royal Free NHS Trust, London
North Middlesex University Hospital NHS Trust, London
St Mary's NHS Trust, London
North Bristol NHS Trust

Other centres

Dept. of Primary Care and Population Sciences, RF&UCMS
Medical Research Council Clinical Trials Unit
Health Protection Agency – Centre for Infections (HPA-CfI)

New centres (2008): St. George's Healthcare NHS Trust, London



Inclusion criteria

Patients

- Aged \geq 16 years
- Seen at any of the centres since 1/1/1996

Centres

- Electronic data already available
- Able to provide data on an annual basis

Funding and location of database

- Study funded by the Medical Research Council since 2001
- Funding provides:
 - Database programmer (part-time)
 - Project coordinator (full-time)
 - Statistician (full-time, from 1/10/04)
 - Small amount of money for centres providing data
- Database located at MRC – centrally located and ‘independent’ of clinical centres
- Project coordinator and principal investigator based at RF&UCMS (academic unit, independent of clinical centre)

Study management

- Study managed by a steering committee, made up of representatives of each clinical centre, the coordinating centres, the data manager and a representative from the UK Resistance Database
- Steering committee meets every 3-6 months
- Data sub-committee created to focus on issues surrounding the merging of data from different centres
- Specific sub-committees (e.g. hepatitis sub-committee) formed as necessary

Methods

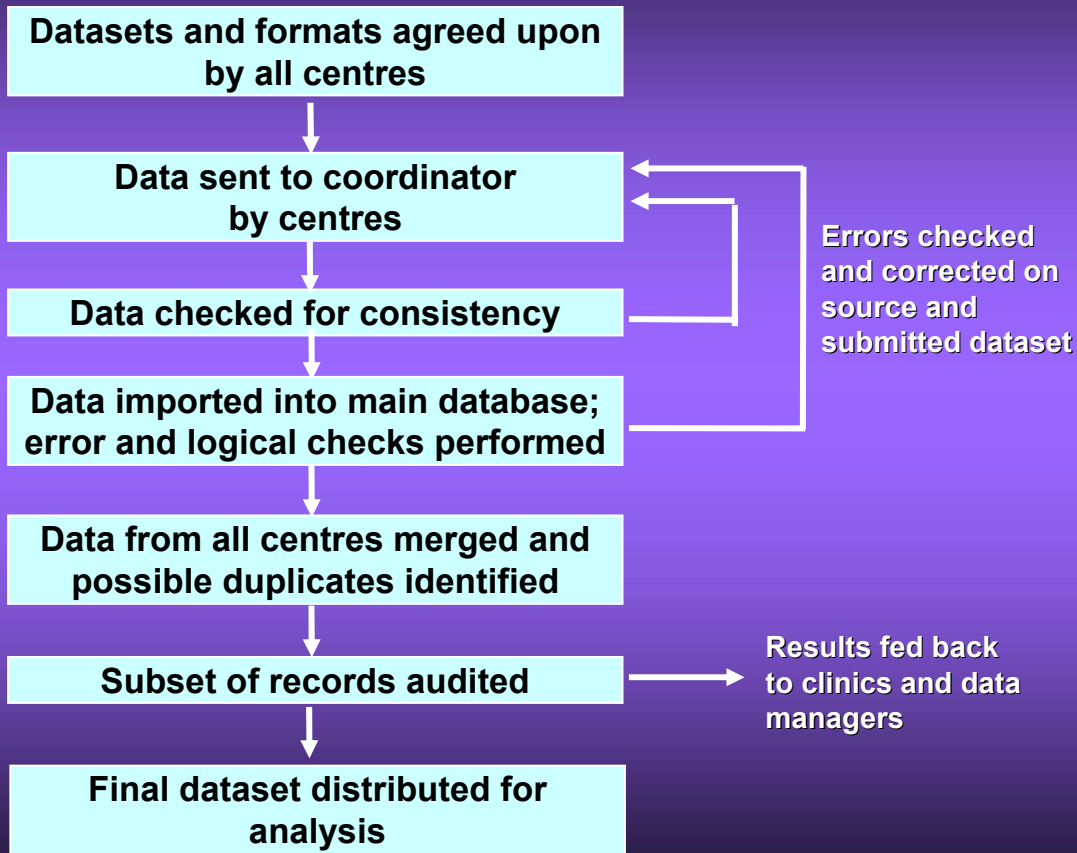
UK CHIC data protection policy

- policy drafted by a sub-group with input from experts in health informatics
- data are submitted by secure web-based transfer (FTP), plus encryption
- database access is restricted and will be monitored
- datasets released for research analyses are approved by the steering committee, are anonymised, and only include necessary data
- personnel with access to the data are made aware of data confidentiality requirements

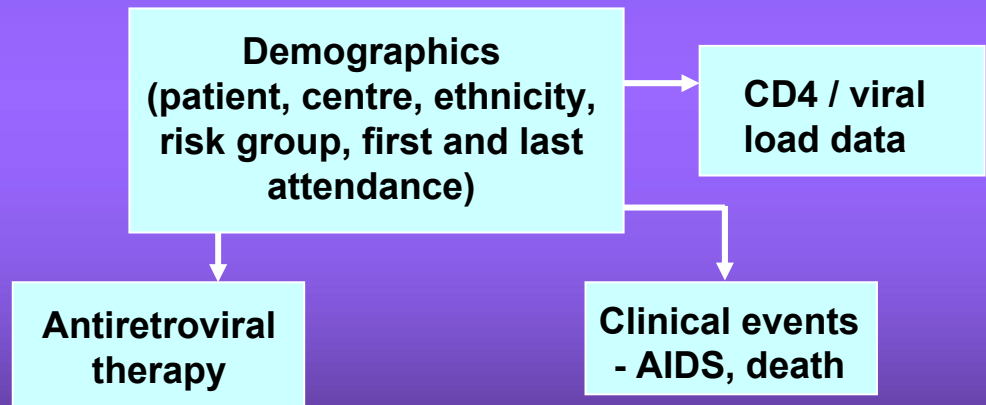
Processes

- Centres provide data on all patients seen at their centre since 1st January 1996
- Data are sent in a pre-agreed electronic format so that they can be easily merged at the coordinating centre
- Includes historic data on each patient prior to 1996 if patient was under follow-up at that time
- *New in 2004:* data were requested on all patients at centre, even if not seen since 1/1/96

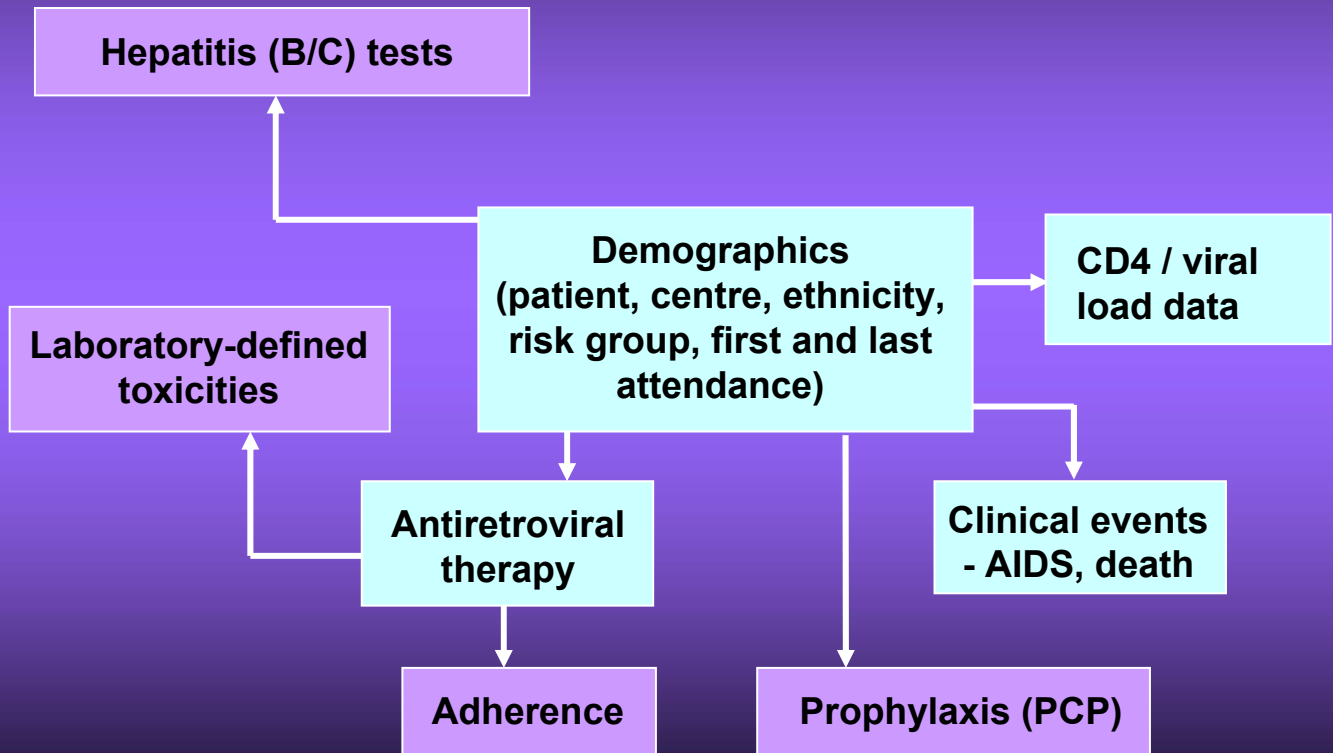
Processes



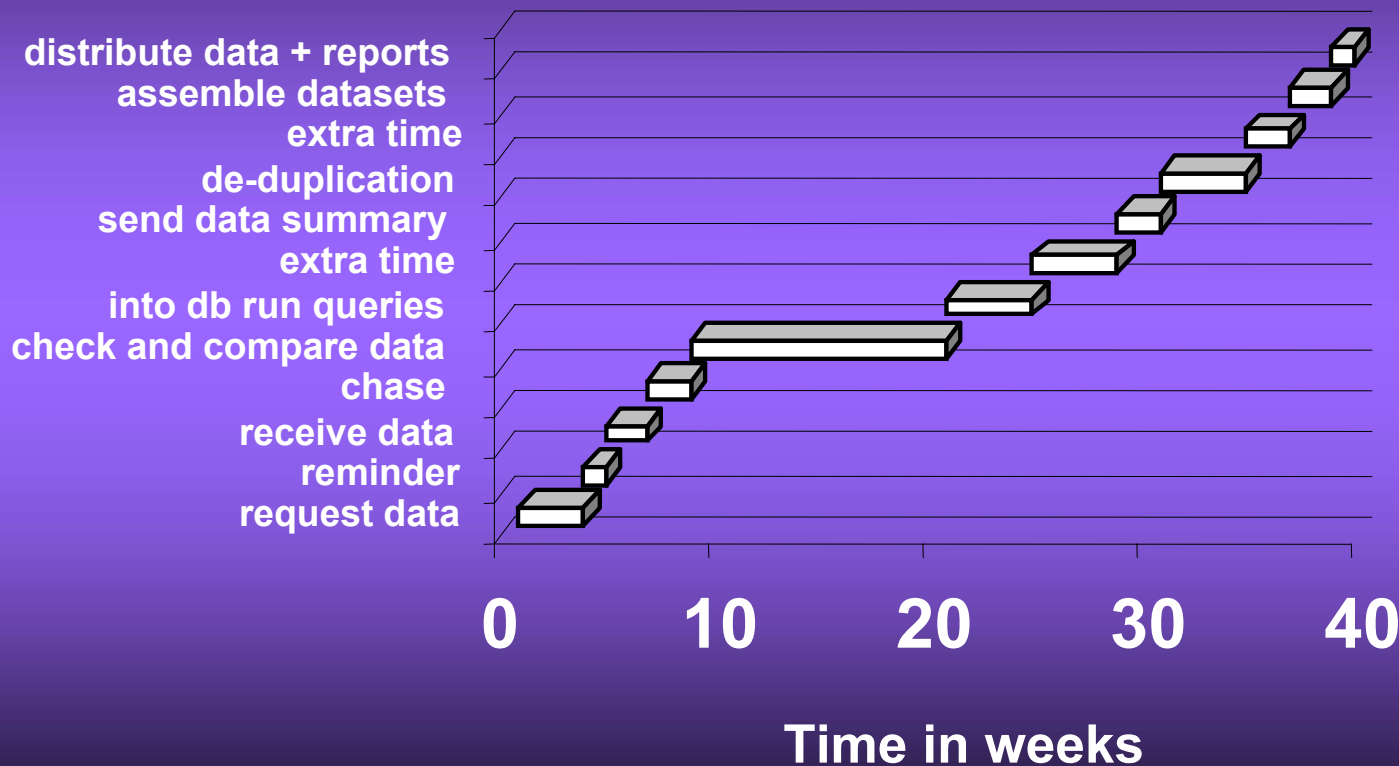
Datasets



Datasets



CHIC agreed timelines



Data quality checks

- Missing data items (demographics, drug names, CD4/CD8 counts, HIV RNA)
- Duplicate patients within same centre
- Duplicate laboratory measurements or AIDS events
- Undetectable viral load at start of treatment
- CD4 or CD8 counts of zero
- Inconsistent data and dates (e.g. HIV+ve date before HIV-ve date, any odd or future dates)
- Overlapping drug start/stop dates

All queries are investigated and both CHIC and clinic databases are updated with corrected information

De-duplication process

- Individuals may have attended more than one clinical centre
- Potential matches identified on basis of matching date of birth and soundex; other demographic variables used to determine whether potential matches are definite or indeterminate, e.g.
 - HIV+ve dates in same calendar year
 - Dates of death within 1 month
 - Transferred to or from same centre
 - First seen and last seen dates are consistent
 - Same country of birth (non-UK only)
- Once duplicate patients have been identified, data from individual records are combined

Improving death data

- Many patients do not 'reappear' at their clinics for long periods of time; some of these may have left the country and/or may have died
- Cohort records are matched to the Office of National Statistics (ONS) list of deaths occurring in individuals aged 16-55 years using soundex, initial, date of birth and sex
- Possible matches are sent to centres to make sure that no evidence exists that patient is still alive; once confirmation is received, database is updated

Audit of data

- 1% of records from each centre audited
- Each record 'recreated' using data obtained from clinical notes and compared with information stored on database (not CD4 or viral load)
- Exact match for demographic data, date to within 1 month for dates of starting ART and AIDS events
- Demographic data generally reasonable (some problems with ethnicity and country of birth); some discrepancies in AIDS events or dates
- Some AIDS events and ARV drugs found in notes but not database and vice versa

Link to UK Resistance database

- UK CHIC linked with UK Collaborative Group on HIV Drug Resistance, set up in 2001 to collect information on routinely performed resistance tests in the UK
- Resistance test data (genotypic and sequence, if available) are collected, plus patient demographics, clinical data, ART and laboratory markers
- Substantial overlap of patients in the two databases so clinical information is shared
- To date, results of over 41,400 resistance tests relating to 28,6920 patients are stored on the database – 13,283 patients have linked clinical data in the UK CHIC study



Key findings

Characteristics of cohort

		n	%
Total number of patients		29055	100.0
Sex:	Female	6954	23.9
Risk group:	Homo/bisexual	15850	54.6
	IDU	1361	4.7
	Heterosexual	9289	32.0
	Other/not known	2555	8.8
Ethnicity:	White	17158	59.1
	Black African	6805	23.4
	Other	3281	11.3
	Not known	1811	6.2
Median (IQR) age at first entry into cohort (years):		31	25-36

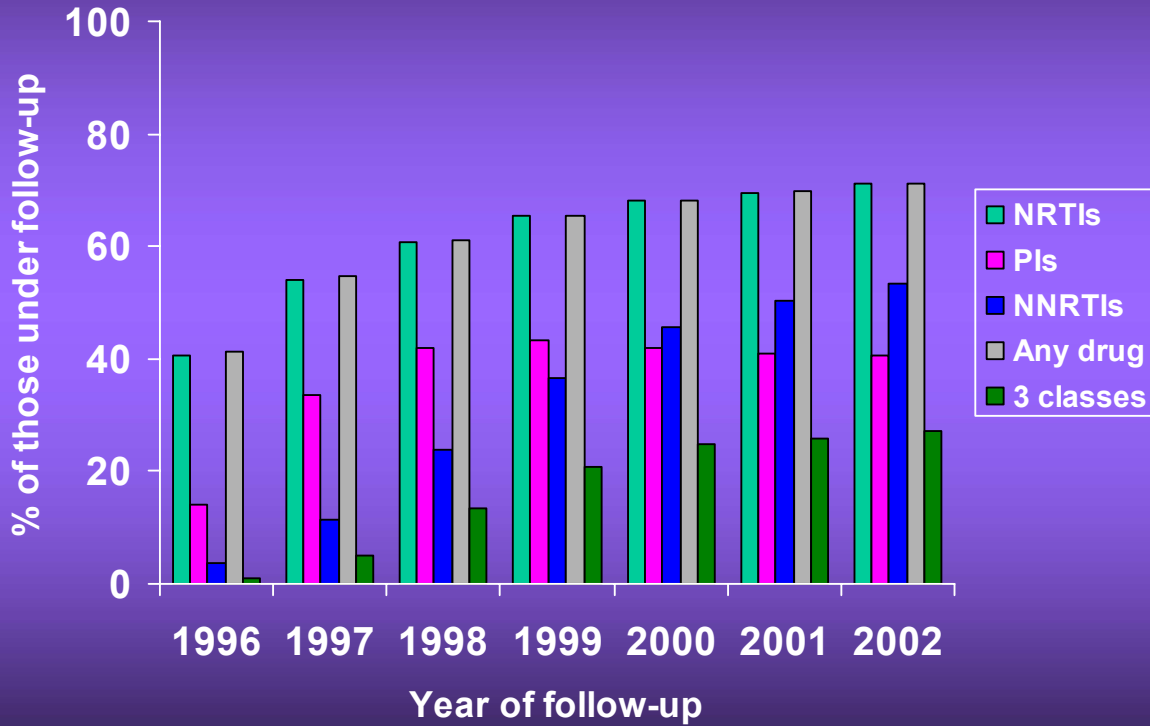
Characteristics of patients under follow-up in each year

Year	Total	Female	Risk group			Ethnicity		Lost to follow-up
			Homo	IDU	Het	White	Black African	
		%	%	%	%	%	%	
1996	9224	14.5	68.9	8.1	15.8	75.1	10.2	-
1997	9718	15.6	67.7	7.5	18.0	74.3	11.6	4.4
1998	10566	16.5	66.7	6.9	20.1	73.5	13.1	3.0
1999	11363	17.5	65.4	6.3	21.9	71.8	14.9	2.9
2000	12329	19.0	63.6	5.6	24.5	69.3	16.9	3.0
2001	13528	20.3	62.2	5.0	26.9	66.8	18.9	3.1
2002	14863	21.4	60.6	4.5	29.2	64.5	20.5	3.2
2003	16060	22.4	59.6	4.2	30.9	63.0	22.1	3.7
2004	17710	23.2	58.9	3.8	32.3	61.5	23.3	4.0
2005	18855	23.5	58.1	3.5	32.9	60.7	10.5	4.4
2006	16688	23.6	57.4	3.3	32.1	60.4	23.8	11.7

Characteristics of patients newly joining the cohort in each year

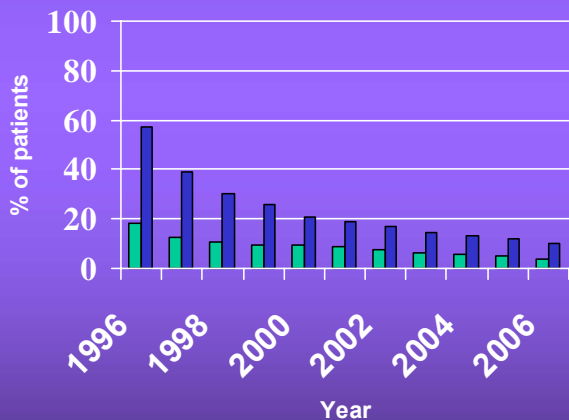
Year	Total	Female	Risk group			Ethnicity		Median CD4 at first visit
			Homo	IDU	Het	White	Black African	
			%	%	%	%	%	
1997	1768	22.0	58.0	5.2	28.1	65.4	19.1	310
1998	1716	22.7	55.1	4.6	32.5	64.3	21.5	310
1999	1625	25.7	51.2	3.3	35.0	57.8	26.7	311
2000	1815	28.4	47.8	2.6	39.6	51.6	29.1	308
2001	2081	30.7	46.7	2.7	43.1	48.1	33.4	320
2002	2241	30.6	44.8	2.5	44.9	45.4	33.8	324
2003	2234	31.3	46.3	2.6	44.3	46.3	34.1	327
2004	2757	30.6	47.7	2.9	44.0	47.4	33.3	316
2005	2385	28.5	46.5	2.4	40.6	49.2	29.3	336
2006	1188	30.5	32.6	2.9	35.0	47.1	30.4	328

Exposure to antiretroviral therapy



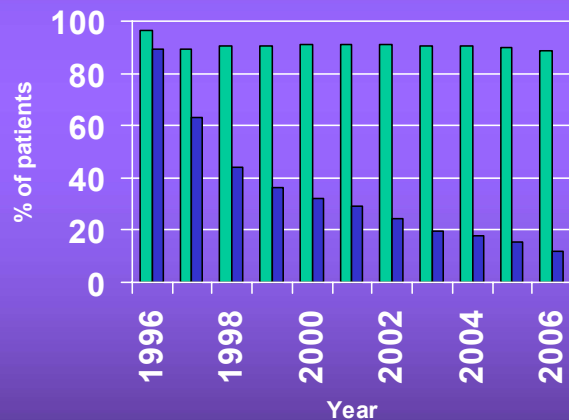
CD4 count and HIV RNA levels of patients under follow-up

a) CD4 <200 cells/mm³



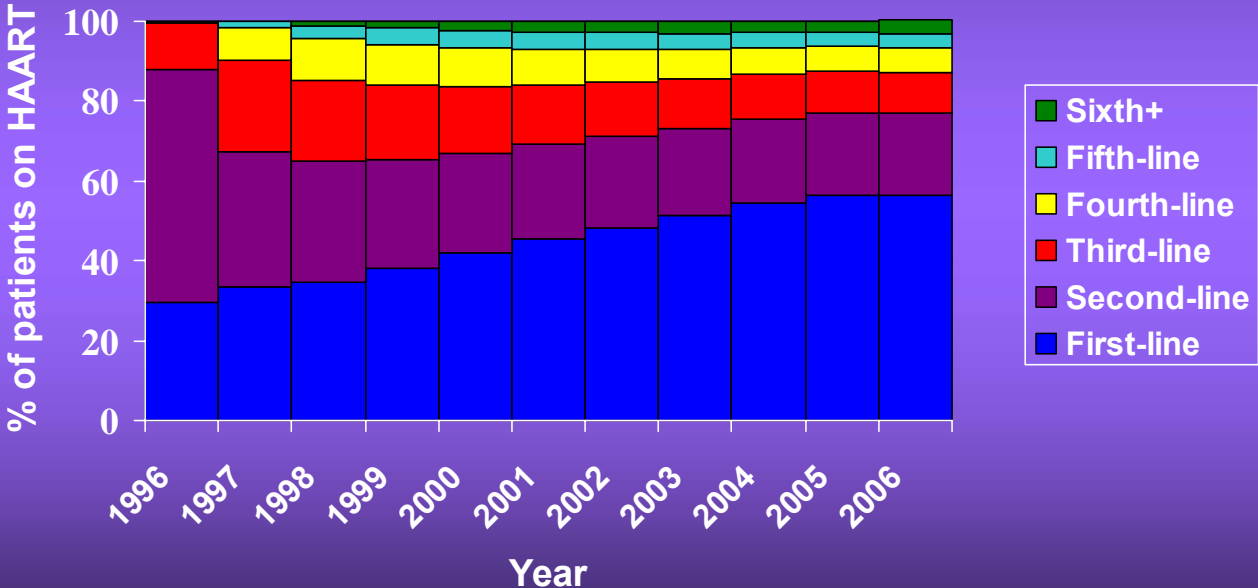
■ Not on treatment ■ On treatment

b) HIV RNA >500 copies/ml

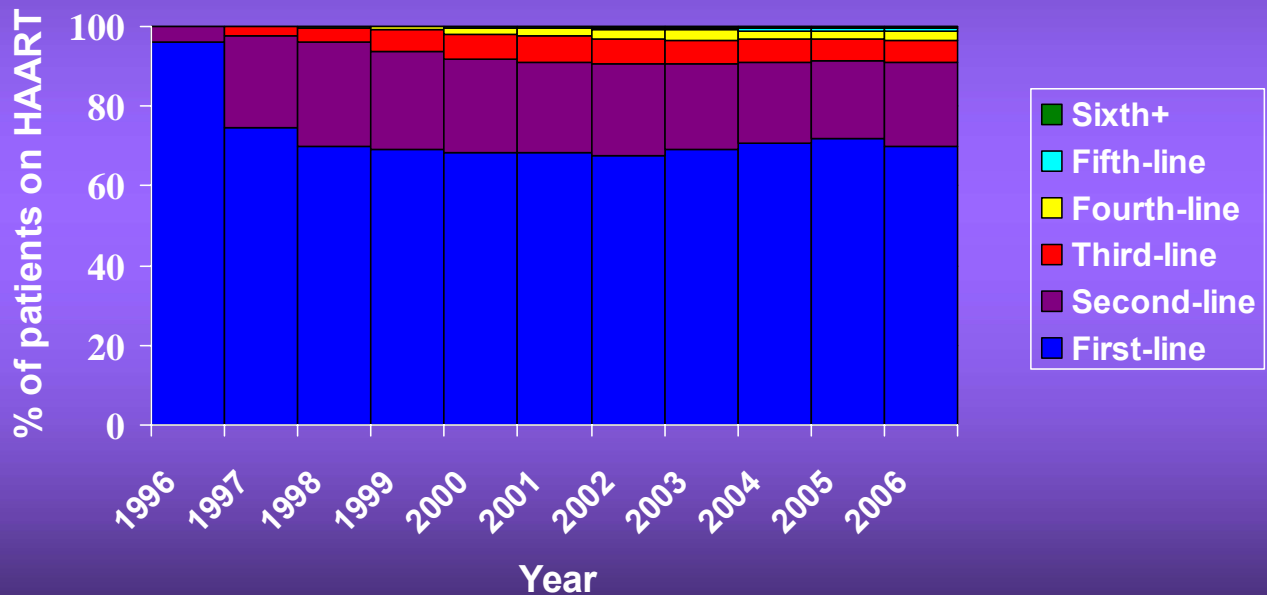


■ Not on treatment ■ On treatment

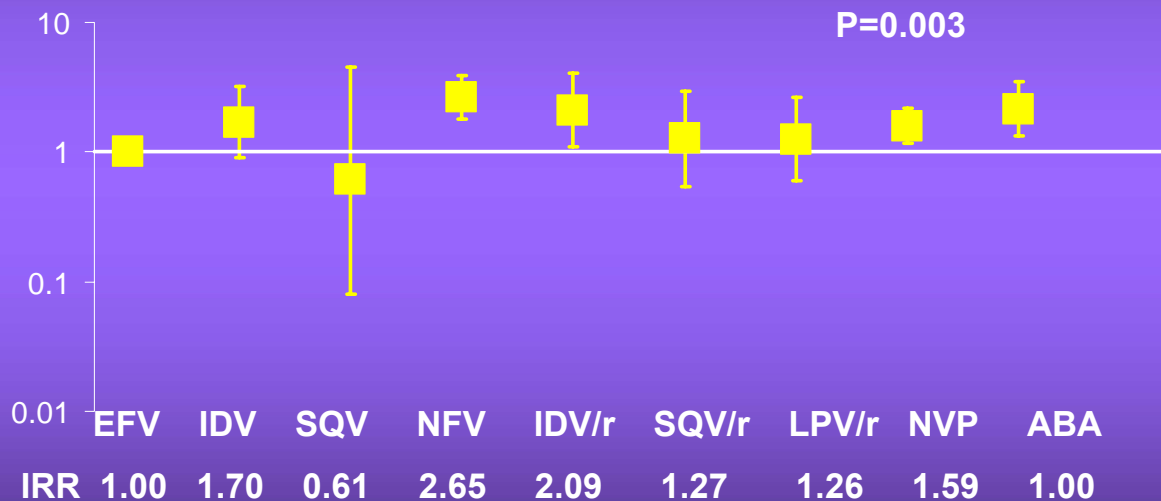
ARV regimens received – all patients under follow-up



ARV regimens received – ARV-naïve patients, CD4 >200 cells/mm³ at start

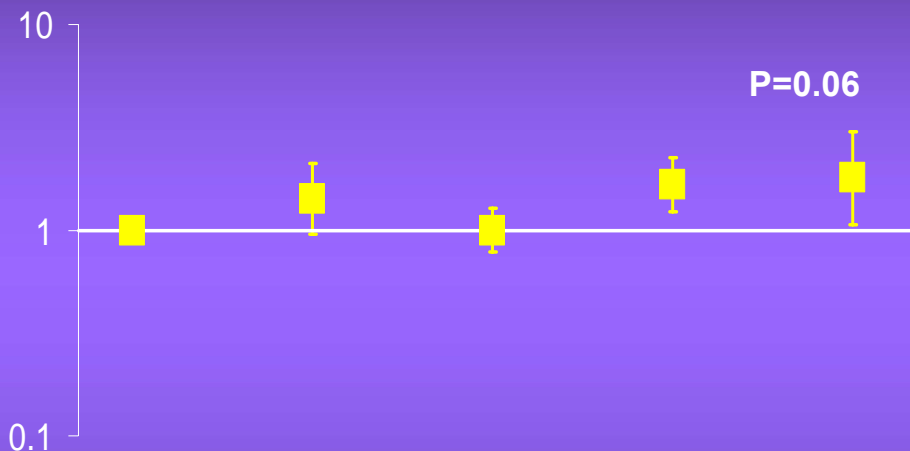


Virological rebound rates according to the 'third' drug in a regimen



Results from multivariable Poisson regression model, adjusted for calendar year, treatment switches, time with viral load <50 copies/ml, CD4 and viral load at HAART, age, race, risk group and sex.

Virological rebound rates according to the NRTI backbone



NRTI	AZT/3TC	AZT/ddI	d4T/3TC	d4T/ddI	Other
IRR	1.00	1.52	1.07	1.73	2.12

Results from multivariable Poisson regression model, adjusted for calendar year, treatment switches, time with viral load <50 copies/ml, CD4 and viral load at HAART, age, race, risk group and sex

Study outputs

Ongoing collaborations

- **Links with Collaborative HIV Paediatric Surveillance (CHIPS) Study and with London HIV Perinatal Research Group (LHPRG)**
- **Liverpool University - therapeutic drug monitoring**
- **London School of Hygiene and Tropical Medicine (LSHTM) - TB incidence in UK**
- **Participation in COHERE Collaboration**
- **Collaborations with statistical research groups to develop statistical methodology for the analysis of observational cohorts**

Published papers from the collaboration (1)

- The UK Collaborative HIV Cohort Steering Committee. The creation of a large UK-based multicentre cohort of HIV-infected individuals: The UK Collaborative HIV Cohort (UK CHIC). *HIV Medicine* 2004; 5: 115-124.
- Sabin CA, Hill T, Lampe F, et al. Treatment exhaustion of highly active antiretroviral therapy (HAART) among individuals infected with HIV in the United Kingdom: multicentre cohort study. *BMJ* 2005; 330: 695.
- Smith CJ, Phillips AN, Hill T, et al. The Rate of Viral Rebound after Attainment of an HIV Load <50 Copies/mL According to Specific Antiretroviral Drugs in Use: Results from a Multicenter Cohort Study. *J Infect Dis* 2005; 192: 1387-97.
- Stöhr W, Dunn D, Porter K, et al. CD4 cell count and initiation of antiretroviral therapy: trends in seven UK centres, 1997-2003. *HIV Med* 2007; 8: 135-41
- Benzie AA, Bansi LK, Sabin CA, et al. Increased duration of viral suppression is associated with lower viral rebound rates in patients with previous treatment failures. *AIDS* 2007; 21: 1423-30.



Published papers from the collaboration (2)

- Phillips AN, Gazzard B, Gilson R, et al. Rate of AIDS diseases or death in HIV-infected antiretroviral therapy-naïve individuals with high CD4 count. *AIDS* 2007; 21: 1717-21.
- Phillips AN, Leen C, Wilson A, et al. Risk of extensive virological failure to the three original antiretroviral drug classes over long-term follow-up from the start of therapy in patients with HIV infection: an observational cohort study. *Lancet* 2007; 370:1923-8.
- Bansi L, Benzie A, Phillips AN, et al. Are prior treatment interruptions associated with higher viral rebound rates in patients with viral suppression? *AIDS (in press)*
- UK CHIC Study Steering Committee. HIV diagnosis at CD4 count above 500/mm³ and progression to below 350/mm³ without antiretroviral therapy. *JAIDS* 2007; 46:275-8.
- Porter D, Walker S, Hill T, et al. Changes in outcome of persons initiating HAART at CD4 < 50 cells/mm³. *JAIDS (in press)*



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