Non-uptake of HAART among patients with a CD4 count <350 cells/mm³ - UK Collaborative HIV Cohort (CHIC)

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BACKGROUND

- Since the introduction of highly active antiretroviral therapy (HAART) in 1996, treatment guidelines have evolved in terms of the CD4 count at which HAART should be initiated
- Current British HIV Association (BHIVA) guidelines (2008) recommend that all patients with a CD4 count <350 cells/mm^3 are offered HAART
- In previous UK CHIC analyses, based on data up to 2003, only 50-60% of patients with a CD4 count <200 cells/mm^3 and 10-15% with a CD4 count of 200-350 cells/mm^3 initiated HAART in the following 6 months.
- Analysis of more recent UK CHIC data has been performed to assess if this situation has now improved.
- We aimed to identify all patients with a confirmed CD4 <350 cells/mm^3 who had still not initiated HAART (any regimen including a PI, NNRTI, abacavir or enfuvirtide) by their last clinic visit in 2007-2009. Patient characteristics were compared to identify factors associated with delayed HAART uptake

METHODS

- All adults fulfilling the following criteria were included in the analysis:
  - A first confirmed (2 consecutive measurements) CD4 count <350 cells/mm^3 measured from 2004-2008
  - At least 6 months follow-up after this count
  - At least 1 clinic visit in 2007-2009
- Demographic (e.g. gender, risk group), clinical (previous AIDS events) and laboratory (CD4 decline, latest viral load, frequency of CD4 monitoring as a surrogate for frequency of attendance) data was used to identify risk factors for failure to initiate HAART
- Analyses used proportional hazards regression with fixed (sex, age, risk group, ethnicity, AIDS, baseline CD4) and time-updated (frequency of CD4, % of CD4 <350 cells/mm^3) covariates

RESULTS

- 5613 patients were identified as having had a confirmed low CD4 <350 cells/mm^3 from 2004-2008 (26% female; 50% MSM, 38% heterosexual; 42% non-white ethnicity; median age 36)
- Of these, 534 (9.5%) had not started HAART by the time of their last clinic visit in 2007-2009
- Median baseline CD4 for the whole cohort was 230 [IQR 117, 300] cells/mm^3
- All patients were followed-up for a median of 28.3 [14.7, 42.4] months and had a median of 12 [7, 17] CD4 counts after baseline of which 60% [33%, 92%] were <350 cells/mm^3

TABLE 1: Factors associated with uptake of HAART – Baseline covariates

		HAART		
		Started	Not started	p-value
Number of patients		5079	534	
Female sex		1343 (26.4)	118 (22.1)	0.03
Risk group	MSM	2493 (49.1)	316 (59.2)	
	IDU	102 (2.0)	13 (2.4)	
	Heterosexual	1978 (38.9)	144 (27.0)	
	Other/not known	506 (10.0)	61 (11.4)	0.0001
Ethnicity	White	2601 (51.2)	295 (55.2)	
	Black African	1532 (30.2)	106 (19.9)	
	Other	635 (12.5)	75 (14.0)	
	Not known	311 (6.1)	58 (10.9)	0.0001
Age (years) at confirmed low CD4 count	Median (IQR)	36 (31, 42)	34 (29, 41)	0.0001
Previous AIDS		546 (10.8)	22 (4.1)	0.0001
First confirmed CD4 count <350 (cells/mm^3)	Median (IQR)	220 (106, 290)	300 (261, 325)	0.0001
Follow-up time (months) after confirmed low count	Median (IQR)	29.2 (15.4, 43.2)	19.6 (10.7, 32.7)	0.0001
Time (days) between first and second CD4 <350 cells/mm^3	Median (IQR)	43 (21, 85)	79 (30, 126)	0.0001
Total number of CD4 count measurements following confirmed low count	Median (IQR)	12 (7, 18)	9 (5, 16)	0.0001
% of these CD4 measures that were <350 cells/mm^3	Median (IQR)	60 (35, 93)	50 (31, 80)	0.0001
Mean time interval (days) between consecutive CD4 measures following confirmed low count	Median (IQR)	86 (67, 109)	108 (80, 149)	0.0001

RESULTS (Continued)

- Multivariable proportional hazards regression analysis of factors associated with HAART uptake was performed. When considering baseline co-variates, those starting HAART were:
  - Older (relative hazard [RH] /10 yrs: 1.12 [95% confidence interval 1.08, 1.15]);
  - More likely to have experienced an AIDS defining illness (1.15 [1.05, 1.26]);
  - And tended to have their low CD4 count in more recent years (RH vs. 2004)
    - 2005: 1.10 [1.01, 1.20]
    - 2006: 1.28 [1.17, 1.39]
    - 2007: 1.46 [1.33, 1.60]
    - 2008: 2.11 [1.91, 2.33]
- Those patients less likely to start HAART included:
  - Intravenous drug users (0.78 [0.63, 0.97])
  - Black African patients (0.85 [0.73, 0.99])
  - And those with a higher baseline CD4 (RH /50 cells 0.71 [0.70, 0.72])

TABLE 2: Results of multivariable proportional hazards regression analysis of factors associated with uptake of HAART (Fixed + time-updated covariates)

		Adjusted	
Factor		RH (95% CI)	p-value
Average of last two CD4 measurements	/50 cells/mm^3 higher	0.56 (0.54, 0.57)	0.0001
Number of CD4 counts after confirmed low value that are <350 cells/mm^3	/count	1.16 (1.14, 1.18)	0.0001
Sex/risk group	MSM	1.08 (0.98, 1.20)	0.13
	Male heterosexual	-	-
	Female heterosexual	1.10 (1.00, 1.21)	0.04
	IDU	0.69 (0.56, 0.87)	0.001
	Male Other	0.82 (0.72, 0.94)	0.005
	Female Other	0.76 (0.64, 0.91)	0.003
Ethnicity	White	1	-
	Black African	0.85 (0.72, 0.99)	0.03
	Other	1.06 (0.97, 1.15)	0.23
	Not known	0.76 (0.62, 0.93)	0.008
Previous AIDS		1.01 (0.92, 1.11)	0.83
Age	/10 years older	1.11 (1.07, 1.14)	0.0001
First confirmed low CD4 count	/50 cells/mm^3 higher	1.22 (1.18, 1.25)	0.0001
Calendar year of confirmed low count	2004	1	-
	2005	1.16 (1.06, 1.26)	0.001
	2006	1.37 (1.26, 1.50)	0.0001
	2007	1.62 (1.48, 1.78)	0.0001
	2008	2.31 (2.08, 2.55)	0.0001

- After controlling for fixed and time-updated covariates, independent predictors for initiation of HAART included:
  - Older age of patient (RH /10 years older 1.11 [1.07, 1.14])
  - A lower average CD4 count when considering the last two measurements taken (RH /50 cells/mm^3 higher 0.56 [0.54, 0.57])
  - A greater number of CD4 counts <350 cells/mm^3 (RH /count 1.16 [1.14, 1.18])
  - Risk group: Female heterosexuals (RH 1.10 [1.00, 1.21]) were more likely to start
- Intravenous drug users remained less likely to start HAART (RH 0.69 [0.56, 0.87])
- The association with the baseline CD4 count was reversed in the final analysis (RH /50 cells/mm^3 higher 1.22 (1.18, 1.25) demonstrating that HAART starters had a more rapidly declining CD4 count

Conclusions

- Since 2004, there has been improvement in the proportion of individuals who are started on HAART once they have had a confirmed CD4 count <350 cells/mm^3
- However, a significant minority of people remain untreated despite clear guidance to the contrary.
- There may be clinician issues influencing access to HAART highlighted in particular by the variation that exists between different risk groups (e.g. IDU vs female heterosexual).
- There appears to be a cohort of patients who first presented with their low CD4 count during the earlier years of this study but who have still not initiated HAART. The data suggests that this group are likely to have a slower rate of decline in their CD4 count.
- American guidance has recently changed to advise starting HAART at CD4 counts greater than 350 cells/mm^3. If, in the future, our guidelines also move in this direction we will need to be even more proactive in increasing access to HAART.
- The main limitation for this study is that data is not collected on any reasons why people don't start, for example, declining HAART.

United Kingdom Collaborative HIV Cohort (UK CHIC)

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