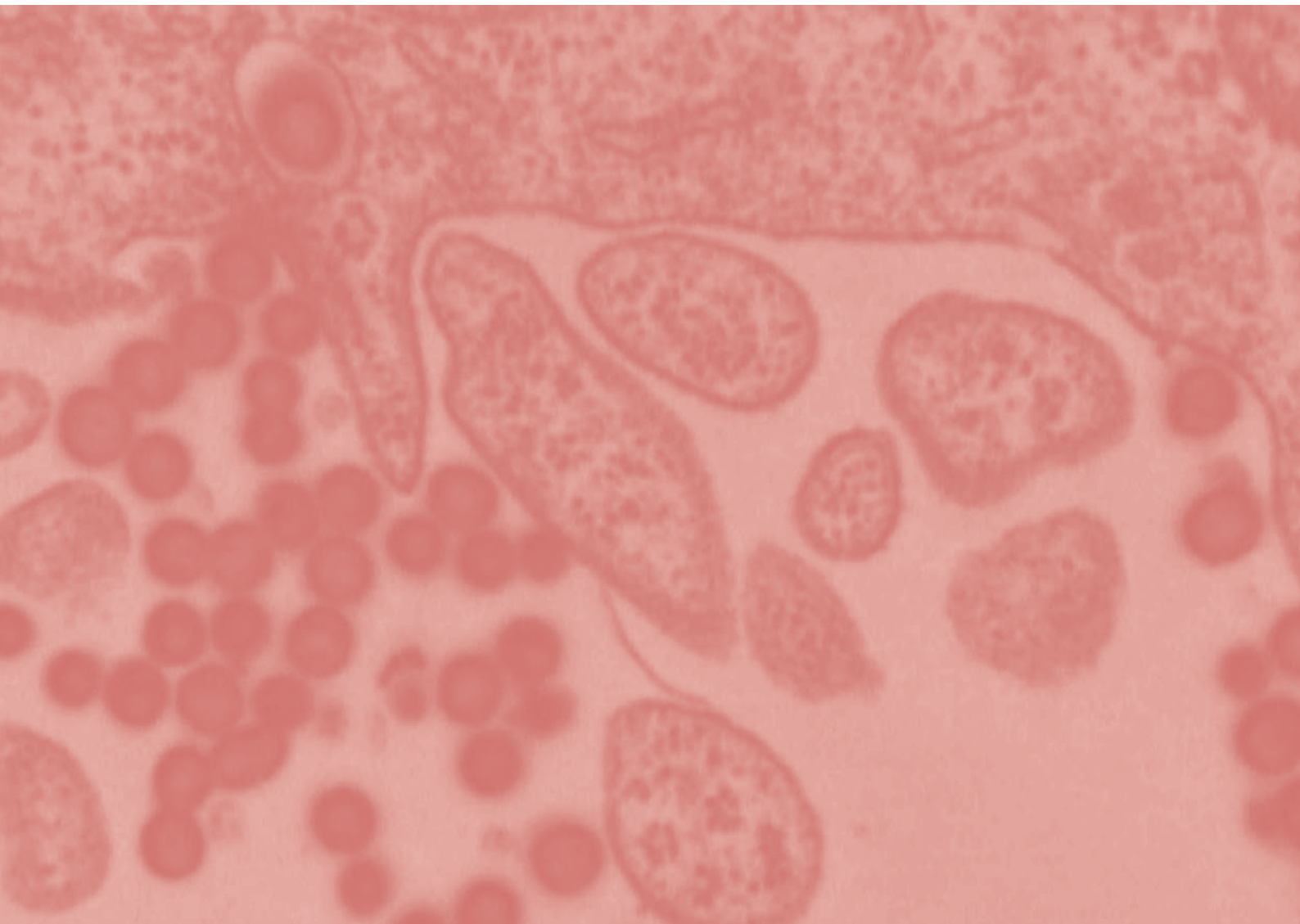


# Chapter 5: CD4 counts and Viral load

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## Ten years of HIV surveillance, CD4 counts and viral load

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### CD4 counts

I bet some people don't even know what the CD stands for, although it's been rolling off the tongue for the last ten years! Well, it means cluster of differentiation and it refers to the antigens that develop on the white cell as it matures into the particular type of cell it's going to be, i.e. a T4 lymphocyte will have antigens on its surface and reacts to a monoclonal antibody that identifies T4 cells and the same goes for T8. In the early days there was a rival company producing monoclonal antibodies and they would have been called leu 2a and 3a. Anyway, that's enough science – I am now getting a headache!

This modern day technology has people rattling off T4 counts like there is no tomorrow and at £70 a test it does require thinking about, but – hey! I remember the bad old days. With your FACS machines and the like; you youngsters don't know you're born. In the eighties a T4 count used to take me nearly two days. I was a Registrar in Immunology in Dublin's fair city. It meant taking gallons of blood, putting it on to a Ficoll Hypaque density gradient, centrifuging the thing for hours, sucking off the buffy layer, washing it in some pink preservative whose name now escapes me, re-suspending the pellet over and over again, and more centrifugation. Then there was the time consuming business of looking down the microscope, counting the cells, switching on and off the fluorescence and pressing a counter. You would have to count more fields than there were in Athenry. At the end of the day the figure you came up with was probably just a good guess! And, you trying telling that to the young people today.....(I wonder how many readers remember the four Yorkshire men and Monty Python).

### As for the viral load

I saw that coming with mounting apprehension. At least it wasn't too bad when you could only get down to a result of less than 400. In those days, we didn't have the constant worry of little blips of 60 and 100 cells. Everything was blissfully under 400 and everybody was happy. Now we are obsessively hand wringing over every little irrelevant blip and sometimes I don't know who's more obsessive – the patients or the doctors? God help us if it ever gets down to fewer than five cells.

However, at least now with all this technology we can try and kid ourselves that managing HIV disease is now a science rather than an art form; but I firmly believe as I get older that intuition, experience, a sixth sense and a hefty scepticism of laboratory results are essential tools in the management of an individual with HIV infection. Luckily, I work in the UK, and even more so – in the North West, where most interventions are contemplated and administered with a large dollop of common sense.

T4 counts and viral loads have been a huge help to us in managing our patients and I have to admit that nothing beats the thrill of seeing a viral load of half a million dropping to five thousand in a month and undetectable at three months. That thrill is heightened even further when a surprise patient actually admits that they feel better now that they are on HAART. It's made me incorporate an additional side effect into the discussion about commencing HAART. Most patients have read and are told all about the gastro-intestinal upset, the diarrhoea, the vivid dreams, and the hypersensitivity, but I always emphasise that one of the common side effects of starting triple therapy is that you might actually feel better!

### What would I like to see for the future?

Well, I'd love the patients to be able to access their own T4 and viral load results. I can easily see computerised access being available so that patients could do this themselves. Indeed, I would hope that many stable patients, either in latent phase or on triple therapy, could almost manage their own condition, with occasional T4/viral load monitoring and prescription collection, as long as everything was stable. This would remove the hassle of finding somewhere to park at a hospital and paying a fortune for it, waiting for hours in a clinic for a blood sample, and then coming back again for another few hours to collect a result, and then deal with the uncertainty of whether the drugs would be ready or not at Pharmacy.

So, from a T4 and viral load point of view, things are looking good and can only get better.

## Background

In 1996 scientists discovered that viral load could predict disease progression. Prior to this only CD4 count was available to measure possible illness<sup>1</sup>. Viral load and CD4 count are two measures used to monitor the health status of individuals with HIV. Viral load has an impact on the CD4 count as an increase of virus in the blood leads to a reduction in CD4 T cells, meaning that there is a greater risk of developing symptomatic HIV in the following years. The results of CD4 counts are shown in cells per cubic millimetre (cells/mm<sup>3</sup>) and the results of viral load tests are shown in copies of HIV RNA per millilitre (copies/ml). HIV is undetectable by most tests below 50 copies/ml, which shows that the test cannot detect HIV in the sample, although this does not mean that the virus is not present<sup>1</sup>.

### *CD4 cell counts*

T-cells (white blood cells) are part of the body's immune system and have CD4 receptors on the surface. The CD4 receptors help T-cells to attach to foreign bodies (antigens). HIV destroys the CD4 T-cells by attaching itself to CD4 receptors and entering the cells. A normal CD4 count of a man without HIV is between 400 and 1,200 cells/mm<sup>3</sup>, and for a woman the normal count is between 500 and 1,600 cells/mm<sup>3</sup>. External forces such as infections, time of the day, smoking, stage in the menstrual cycle, oral contraceptive use, rest and stress can affect CD4 counts<sup>1</sup>. Once measuring CD4 counts became a routine part of care for HIV positive individuals, the Health Protection Agency (HPA) began a surveillance scheme (in 1993) to monitor the CD4 count of the HIV positive population. The CD4 cell count data are longitudinal and monitor trends in immunosuppression in individuals with HIV<sup>2</sup>. The HPA's analyses show that the proportion of people at high risk of opportunistic infection (the proportion with a minimum CD4 count of <200 cells/mm<sup>3</sup>) by year of diagnosis for different cohorts increased until 1996 when antiretroviral therapy became widely available, after which the proportion has steadily decreased. These types of analyses are useful in seeing any trends in CD4 count (for example, an increase in the proportion of those with low CD4 counts), which may indicate failing treatment for those on long-term antiretroviral therapy<sup>3</sup>. Both CD4 count and viral load are important in predicting long term outcome of HIV disease. Researchers in Canada recently found that patients on treatment who achieve viral load suppression but not an increase in CD4 count to 200 cell/mm<sup>3</sup> or above, have an increased rate of clinical HIV symptoms in the first year of treatment. If the CD4 count did not increase after a year of treatment then there was a trend for an increase in clinical HIV symptoms<sup>4</sup>.

### *Viral load*

Viral load is a measurement of the quantity of virus, taken from blood samples. It is used as a marker of disease progression. An increase in viral load is often followed by a fall in CD4 count, which is frequently followed by an illness. Viral load can be affected by a number of external factors such as vaccinations and infections and it is also possible that the time of day the test is taken makes a difference. It is therefore important for individuals with HIV and their physicians to look at the trend of viral load over time rather than the results of a single test<sup>1</sup>.

Various studies have been conducted to predict prognosis of HIV infection with viral load. A study in 1998 looked at the difference between sexes regarding HIV viral load and progression to AIDS amongst a group of HIV infected drug users. Viral load was found to be lower in females than males who had similar CD4 counts. There was also a relatively higher risk for females developing AIDS<sup>5</sup>. In response, researchers involved in the Swiss HIV Cohort Study suggested that data from cohorts other than injecting drug users with HIV be used before treatment for females with HIV are reconsidered or altered as a result of the findings. They looked at the relationship between viral load and CD4 count of those infected through injecting drug use and heterosexual sex and found that there were similar results for males and females<sup>6</sup>. A further study looked at viral load and CD4 cell count as prognostic indicators for AIDS. This study found that viral load had better predictive value than CD4 count measures. However, viral load measures combined with CD4 count measures were very powerful predictors for progression to AIDS in the cohort of mainly African-American injecting drug users with HIV<sup>7</sup>.

One of the preferable outcomes for HIV treatment is an undetectable viral load<sup>8</sup>. The virological response to antiretroviral therapy after 24 weeks of treatment can be predicted by earlier measurements (at four weeks), thus enabling monitoring and investigation of possible reasons for treatment failure (which may include adherence difficulties, tolerability of drugs, level of drugs and drug resistance)<sup>9</sup>.

## Aims of this study

The aims of the analysis in this chapter are to investigate relationships between CD4 count and viral load in HIV positive people in the North West of England and to identify whether a low CD4 count or a detectable viral load can be predicted using age, sex, ethnicity, route of infection, stage, deprivation, whether the individual is new to the treatment and care database, stays in hospital and antiretroviral therapy.

## Methodology

Treatment and care data for 2005 were extracted from the North West HIV/AIDS Monitoring Unit's database. Using residence data, individuals were matched to lower super output area (LSOA) and subsequently to deprivation score

(3,563 individuals, 85% of those seen in the region in 2005). These included all those for whom data on residence was available, but only those who resided within the North West region. The deprivation scores used were the 2004 indices of multiple deprivation<sup>10</sup> and were split into three categories; i.e. most affluent (scores between 1 and 30), intermediate (scores between 31 and 54) and poorest (scores between 55 and 86). Following this, anyone without a CD4 count and/or a viral load were excluded from the dataset, leaving 2,319 individuals (55% of those seen in 2005). There were 2,257 individuals with both a CD4 count and a viral load.

Three binary logistic regression models were run to predict:

- A CD4 count of less than 200 cells/mm<sup>3</sup>;
- A viral load of more than 50 copies/ml; and
- Both a CD4 count of less than 200 cells/mm<sup>3</sup> and a viral load of 10,000 copies/ml or more.

The categories of CD4 count (<200 and 200 or more cells/mm<sup>3</sup>) were chosen as it is recommended that antiretroviral therapy be commenced before an individual's CD4 count falls below 200 cells/mm<sup>3</sup>, and in any individual with a CD4 count of less than 200 cells/mm<sup>3</sup> at diagnosis<sup>8</sup>. The viral load categories (<50 copies/ml and 50 or more copies/ml) were chosen because the measurement of success of an antiretroviral therapy regime is achieving an undetectable viral load (<50 copies/ml)<sup>1,8</sup>. However, people can have a detectable viral load and still be healthy: amongst asymptomatic individuals, a viral load below 10,000 copies/ml is considered low and above 100,000 copies/ml is considered high<sup>1</sup>. A viral load of above 1,000 copies/ml measured four weeks after commencing therapy is cause for concern in terms of patient adherence and possible drug resistance and a failure to reach below 1,000 copies/ml after four weeks is associated with failure to achieve an undetectable viral load within 24 weeks<sup>9</sup>. Therefore, a viral load of greater than 50 copies/ml was chosen as a measurement of potential ill-health, even though someone with a viral load of up to 10,000 copies/ml can still be healthy. In order to check that the results were similar using a higher cut off, the analyses were repeated using categories of <10,000 copies/ml and 10,000 or more copies/ml (these analyses yielded similar results and are not presented here). The third logistic regression model was used to investigate the relationships with the variables for the individuals who have both a low CD4 count (<200 cells/mm<sup>3</sup>) and a higher viral load (10,000 copies/ml or more).

The variables entered into the model were: age group, sex, ethnicity, infection route, stage of disease, deprivation, whether or not an individual was new to the database in 2005, whether or not they had required a stay in hospital, whether they were on antiretroviral therapy and CD4 count/viral load. For an explanation of statistical and technical terms, see the glossary.

## Results

**Table 5.1** shows that there is a significant relationship between CD4 count and viral load. In general, those with lower CD4 counts had higher viral loads. There were 170 individuals (8% of all individuals in the analysis) with a CD4 count of <200 cells/mm<sup>3</sup> and a viral load of 10,000 copies/ml or more. Those with higher CD4 counts (200 cells/mm<sup>3</sup> or more) were almost equally split between viral load category.

**Table 5.2**, the logistic regression model predicting a CD4 count of <200 cells/mm<sup>3</sup>, shows that (after accounting for all the other variables) route of infection, stage of disease, deprivation, being new to the database, whether a patient was on antiretroviral therapy (ART) and whether a patient had a viral load of 50 or more, were significant.

Those who acquired their infection through injecting drug use (IDU), heterosexual sex and blood/tissue were all more likely (adjusted odds ratios 4.18, 1.89 and 2.05, respectively) than those who had acquired their infection through sex between men (MSM) to have a CD4 count of less than 200 cells/mm<sup>3</sup>. Those living in the poorest areas were more likely (adjusted odds ratio 1.57) than those living in the most affluent areas to have a CD4 count of less than 200 cells/mm<sup>3</sup>.

Individuals whose stage of disease was symptomatic, AIDS, had died from AIDS or whose stage was unknown, were more likely to have a CD4 count of less than 200 cells/mm<sup>3</sup> than those who were asymptomatic. Patients who were new to the North West HIV treatment and care database (not necessarily newly diagnosed) were more likely (adjusted odds ratio 3.53) to have a CD4 count of less than 200. Those individuals on ART were more likely to have a CD4 count of less than 200 (adjusted odds ratio 5.46) compared to those not on ART. Those with a viral load of 50 or more were more likely than those with a viral load of less than 50 to have a CD4 count of less than 200 cells/mm<sup>3</sup>.

Females and individuals from black and minority ethnic (BME) communities were more likely to have low CD4 counts, as revealed by the significant univariate relationships (see left hand columns of table 5.2). However, these relationships did not remain significant after accounting for the other variables in the multivariate analysis.

**Table 5.3**, the logistic regression model predicting a viral load of 50 or more copies/ml, showed that (after accounting for all the other variables) route of infection, deprivation, whether or not a patient was new to the

database, stays in hospital, whether the patient was on ART and whether they had a CD4 count of less than 200 cells/mm<sup>3</sup>, were significant.

Those patients infected through heterosexual sex were less likely (adjusted odds ratios 0.54) than those infected through MSM to have a viral load of 50 or more. Individuals living in the poorest areas were more likely (adjusted odds ratio 1.51) than those living in the most affluent (least deprived) areas to have a viral load of 50 or more.

Patients who had stayed a night or more in hospital were more likely (adjusted odds ratio 1.87) than those who had not to have a viral load of 50 or more copies/ml. Those individuals on ART were less likely (adjusted odds ratio 0.03) to have a viral load of 50 or more compared to those not on ART. Those with a CD4 count of less than 200 cells/mm<sup>3</sup> were more likely (adjusted odds ratio 1.99) than those with a higher CD4 count to have a viral load of 50 copies/ml or more.

Age group was highly significant in the univariate analysis (see left hand columns, table 5.3) with proportions of those with a detectable viral load decreasing with increasing age group. However, age group did not remain significant in the multivariate analysis.

Further analyses were conducted to check that the results were similar using a higher viral load cut off. The analyses were repeated using categories of less than 10,000 copies/ml and 10,000 or more copies/ml. The patterns were similar except that sex and stage of disease became significant in the multivariate analysis (people who had received an AIDS diagnosis in the past were less likely to have a higher viral load than those who were asymptomatic and females were more likely than males to have a higher viral load; results not displayed here).

**Table 5.4** shows predictors for having a CD4 count of less than 200 cells/mm<sup>3</sup> and a viral load of 10,000 copies/ml or more. After accounting for all other variables, stage of disease, deprivation, whether an individual was new to the database, stays in hospital and whether an individual was on antiretroviral therapy were all found to be predictors of both a low CD4 count (less than 200) and a high viral load (10,000 or more) and, therefore, predictors of possible ill-health.

Individuals living in the poorest areas were more likely (adjusted odds ratio 1.94) than those living in the most affluent areas to have a low CD4 count and a higher viral load.

Those individuals with an AIDS diagnosis were more likely (adjusted odds ratio 2.13) than those who were asymptomatic to have a CD4 count of less than 200 cells/mm<sup>3</sup> and a viral load of 10,000 copies/ml or more. People who were new to the database in 2005 were more likely than existing people (adjusted odds ratio 5.61) to have a low CD4 count and high viral load. Also, those who required a stay in hospital were more likely than those who had not (adjusted odds ratio 1.82) to have a CD4 count of less than 200 cells/mm<sup>3</sup> and a viral load of 10,000 copies/ml or more. Those on antiretroviral therapy were more likely than those not on therapy (adjusted odds ratio 2.38) to have a low CD4 count and high viral load.

**Table 5.1:** Relationship between CD4 count and viral load

	Viral load (copies/ml)			Total	Chi square	df	P value
	<50	50-10000	10000+				
<b>CD4 Count (cells/mm<sup>3</sup>)</b>					<b>18.2</b>	<b>2</b>	<b>&lt;0.001</b>
200+	629 (33.4%)	616 (32.7%)	638 (33.9%)	1883			
<200	104 (27.8%)	100 (26.7%)	170 (45.5%)	374			
<b>Total</b>	<b>733 (32.5%)</b>	<b>716 (31.7%)</b>	<b>808 (35.8%)</b>	<b>2257</b>			

**Table 5.2:** Logistic regression model predicting a CD4 count of <200 cell/mm<sup>3</sup>

Variable	n	CD4 <200	Univariate			Multivariate	
			Chi square	df	P value	Adj OR (95% CI)	P value
<b>Age group</b>			<b>1.7</b>	<b>4</b>	<b>0.786</b>		<b>0.886</b>
0-14	23	3 (13%)				Reference category	
15-29	425	67 (15.8%)				1.38 (0.11 - 17.73)	0.804
30-44	1305	216 (16.6%)				1.26 (0.1 - 16.54)	0.858
45-59	456	81 (17.8%)				1.14 (0.09 - 15.06)	0.923
60+	83	17 (20.5%)				1.05 (0.07 - 14.67)	0.974
<b>Sex</b>			<b>5.4</b>	<b>1</b>	<b>0.020</b>		<b>0.328</b>
Male	1730	272 (15.7%)				Reference category	
Female	562	112 (19.9%)				0.83 (0.58 - 1.2)	
<b>Ethnicity</b>			<b>10.1</b>	<b>2</b>	<b>0.006</b>		<b>0.553</b>
White	1607	244 (15.2%)				Reference category	
BME	683	140 (20.5%)				0.81 (0.55 - 1.19)	0.276
Unknown	2					0 (0.000 - .)	0.999
<b>Route of infection</b>			<b>38.0</b>	<b>5</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
MSM	1304	170 (13%)				Reference category	
Injecting drug use	41	15 (36.6%)				4.18 (1.93 - 9.02)	<0.001
Heterosexual	848	177 (20.9%)				1.89 (1.27 - 2.83)	0.002
Blood/tissue	52	12 (23.1%)				2.05 (1.01 - 4.18)	0.048
Mother to child	25	4 (16%)				1.53 (0.15 - 15.6)	0.719
Unknown	22	6 (27.3%)				2.47 (0.84 - 7.22)	0.099
<b>Stage of disease</b>			<b>131.0</b>	<b>5</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
Asymptomatic	1109	114 (10.3%)				Reference category	
Symptomatic	652	109 (16.7%)				1.63 (1.17 - 2.29)	0.004
AIDS	435	135 (31%)				3 (2.11 - 4.26)	<0.001
AIDS related death	11	9 (81.8%)				13.71 (2.24 - 83.91)	0.005
Death unrelated to AIDS	5	1 (20%)				0 (0.000 - .)	0.999
Unknown	80	16 (20%)				2.17 (1.15 - 4.11)	0.017
<b>Deprivation*</b>			<b>16.6</b>	<b>2</b>	<b>&lt;0.001</b>		<b>0.006</b>
Most affluent (least deprived)	767	109 (14.2%)				Reference category	
Intermediate	762	113 (14.8%)				1.06 (0.77 - 1.46)	0.741
Poorest (most deprived)	763	162 (21.2%)				1.57 (1.15 - 2.14)	0.005
<b>New to the database in 2005</b>			<b>49.4</b>	<b>1</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
Not new to the database	1716	233 (13.6%)				Reference category	
New to the database	576	151 (26.2%)				3.53 (2.59 - 4.81)	
<b>Inpatient stays</b>			<b>62.7</b>	<b>1</b>	<b>&lt;0.001</b>		<b>0.098</b>
No stays	2086	309 (14.8%)				Reference category	
1 or more nights in hospital	206	75 (36.4%)				1.38 (0.94 - 2.03)	
<b>Antiretroviral therapy (ART)</b>			<b>93.8</b>	<b>1</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
Not on ART	838	57 (6.8%)				Reference category	
On ART	1454	327 (22.5%)				5.46 (3.77 - 7.92)	
<b>Viral load</b>			<b>4.5</b>	<b>1</b>	<b>0.035</b>		<b>&lt;0.001</b>
<50	733	104 (14.2%)				Reference category	
50+	1524	270 (17.7%)				1.94 (1.46 - 2.58)	
Viral load total**	2257	374 (16.6%)					
<b>Total</b>	<b>2292</b>	<b>384 (16.8%)</b>					

\* Deprivation score ranges: most affluent (least deprived) 1-30, intermediate 31-54 and poorest (most deprived) 55-86.

\*\* The viral load total does not match the CD4 count total as not all individuals in the analysis had both a CD4 count and a viral load.

**Table 5.3:** Logistic regression model predicting a viral load of 50 copies/ml or more

Variable	n	VL 50+	Univariate			Multivariate	
			Chi square	df	P value	Adj OR (95% CI)	P value
<b>Age group</b>			<b>92.5</b>	<b>4</b>	<b>&lt;0.001</b>		<b>0.222</b>
0-14	26	22 (84.6%)				Reference category	
15-29	422	353 (83.6%)				0.25 (0.02 - 4.38)	0.345
30-44	1293	860 (66.5%)				0.19 (0.01 - 3.33)	0.255
45-59	460	273 (59.3%)				0.19 (0.01 - 3.29)	0.250
60+	83	35 (42.2%)				0.13 (0.01 - 2.45)	0.175
<b>Sex</b>			<b>0.7</b>	<b>1</b>	<b>0.407</b>		<b>0.924</b>
Male	1726	1174 (68%)				Reference category	
Female	558	369 (66.1%)				0.98 (0.7 - 1.39)	
<b>Ethnicity</b>			<b>0.8</b>	<b>2</b>	<b>0.664</b>		<b>0.654</b>
White	1602	1075 (67.1%)				Reference category	
BME	680	467 (68.7%)				1.08 (0.77 - 1.51)	0.662
Unknown	2	1 (50%)				0.07 (0 - 48.4)	0.422
<b>Route of infection</b>			<b>33.3</b>	<b>5</b>	<b>&lt;0.001</b>		<b>0.015</b>
MSM	1302	920 (70.7%)				Reference category	
Injecting drug use	38	22 (57.9%)				0.62 (0.29 - 1.37)	0.238
Heterosexual	841	536 (63.7%)				0.54 (0.38 - 0.77)	0.001
Blood/tissue	53	23 (43.4%)				0.61 (0.32 - 1.13)	0.115
Mother to child	28	23 (82.1%)				0.55 (0.04 - 7.75)	0.656
Unknown	22	19 (86.4%)				1.48 (0.36 - 6.12)	0.586
<b>Stage of disease</b>			<b>170.1</b>	<b>5</b>	<b>&lt;0.001</b>		<b>0.084</b>
Asymptomatic	1102	880 (79.9%)				Reference category	
Symptomatic	655	355 (54.2%)				0.82 (0.62 - 1.07)	0.148
AIDS	434	236 (54.4%)				0.94 (0.69 - 1.27)	0.663
AIDS related death	9	5 (55.6%)				0.21 (0.04 - 1.17)	0.075
Death unrelated to AIDS	4	3 (75%)				1.15 (0.07 - 19.93)	0.926
Unknown	80	64 (80%)				1.76 (0.92 - 3.36)	0.087
<b>Deprivation*</b>			<b>23.3</b>	<b>2</b>	<b>&lt;0.001</b>		<b>0.003</b>
Most affluent (least deprived)	763	472 (61.9%)				Reference category	
Intermediate	764	515 (67.4%)				1 (0.77 - 1.31)	0.990
Poorest (most deprived)	757	556 (73.4%)				1.51 (1.15 - 1.98)	0.003
<b>New to the database in 2005</b>			<b>164.5</b>	<b>1</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
Not new to the database	1709	1030 (60.3%)				Reference category	
New to the database	575	513 (89.2%)				3.21 (2.28 - 4.51)	
<b>Inpatient stays</b>			<b>5.2</b>	<b>1</b>	<b>0.022</b>		<b>0.002</b>
No stays	2082	1392 (66.9%)				Reference category	
1 or more nights in hospital	202	151 (74.8%)				1.87 (1.26 - 2.79)	
<b>Antiretroviral therapy (ART)</b>			<b>525.0</b>	<b>1</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
Not on ART	835	811 (97.1%)				Reference category	
On ART	1449	732 (50.5%)				0.03 (0.02 - 0.05)	
<b>CD4 count</b>			<b>4.5</b>	<b>1</b>	<b>0.035</b>		<b>&lt;0.001</b>
200+	1883	1254 (66.6%)				Reference category	
<200	374	270 (72.2%)				1.99 (1.5 - 2.65)	
CD4 Total**	2257	1524 (67.5%)					
<b>Total</b>	<b>2284</b>	<b>1543 (67.6%)</b>					

\*Deprivation score ranges: most affluent (least deprived) 1-30, intermediate 31-54 and poorest (most deprived) 55-86.

\*\*The CD4 total does not match the viral load total as not all individuals in the analysis had both a CD4 count and a viral load.

**Table 5.4:** Logistic regression model predicting a CD4 count of <200 cells/mm<sup>3</sup> and a viral load of 10,000 copies/ml or more

Variable	n	CD4 <200 and VL 10,000+	Univariate			Multivariate	
			Chi square	df	P value	Adj OR (95%CI)	P value
<b>Age group</b>			<b>4.7</b>	<b>4</b>	<b>0.315</b>		<b>0.725</b>
0-14	26	3 (11.5%)				Reference category	
15-29	429	41 (9.6%)				0.41 (0.02 - 7.93)	0.554
30-44	1316	88 (6.7%)				0.31 (0.02 - 6.19)	0.446
45-59	464	32 (6.9%)				0.3 (0.02 - 6.04)	0.430
60+	84	6 (7.1%)				0.31 (0.01 - 6.99)	0.462
<b>Sex</b>			<b>3.0</b>	<b>1</b>	<b>0.085</b>		<b>0.389</b>
Male	1750	119 (6.8%)				Reference category	
Female	569	51 (9%)				0.81 (0.49 - 1.32)	
<b>Ethnicity</b>			<b>15.3</b>	<b>2</b>	<b>&lt;0.001</b>		<b>0.770</b>
White	1626	97 (6%)				Reference category	
BME	691	73 (10.6%)				1.22 (0.71 - 2.11)	0.470
Unknown	2	0 (0%)				0 (0.000 - .)	0.999
<b>Route of infection</b>			<b>14.0</b>	<b>5</b>	<b>0.016</b>		<b>0.795</b>
MSM	1318	78 (5.9%)				Reference category	
Injecting drug use	42	4 (9.5%)				1.3 (0.41 - 4.14)	0.653
Heterosexual	856	79 (9.2%)				1.08 (0.6 - 1.92)	0.801
Blood/tissue	53	2 (3.8%)				0.94 (0.22 - 4.04)	0.932
Mother to child	28	3 (10.7%)				0.46 (0.02 - 8.85)	0.607
Unknown	22	4 (18.2%)				2.21 (0.65 - 7.52)	0.205
<b>Stage of disease</b>			<b>30.0</b>	<b>5</b>	<b>&lt;0.001</b>		<b>0.003</b>
Asymptomatic	1119	64 (5.7%)				Reference category	
Symptomatic	663	41 (6.2%)				1.39 (0.87 - 2.22)	0.166
AIDS	439	49 (11.2%)				2.13 (1.32 - 3.45)	0.002
AIDS related death	12	3 (25%)				2.27 (0.47 - 10.85)	0.306
Death unrelated to AIDS	5					0 (0.000 - .)	0.999
Unknown	81	13 (16%)				3.72 (1.82 - 7.61)	<0.001
<b>Deprivation*</b>			<b>20.2</b>	<b>2</b>	<b>&lt;0.001</b>		<b>0.006</b>
Most affluent (least deprived)	773	37 (4.8%)				Reference category	
Intermediate	773	51 (6.6%)				1.25 (0.78 - 2)	0.347
Poorest (most deprived)	773	82 (10.6%)				1.94 (1.25 - 3.03)	0.003
<b>New to the database in 2005</b>			<b>102.6</b>	<b>1</b>	<b>&lt;0.001</b>		<b>&lt;0.001</b>
Not new to the database	1735	72 (4.1%)				Reference category	
New to the database	584	98 (16.8%)				5.61 (3.84 - 8.21)	
<b>Inpatient stays</b>			<b>39.0</b>	<b>1</b>	<b>&lt;0.001</b>		<b>0.013</b>
No stays	2108	132 (6.3%)				Reference category	
1 or more nights in hospital	211	38 (18%)				1.82 (1.14 - 2.92)	
<b>Antiretroviral therapy</b>			<b>11.4</b>	<b>1</b>	<b>0.001</b>		<b>&lt;0.001</b>
Not on ART	851	42 (4.9%)				Reference category	
On ART	1468	128 (8.7%)				2.38 (1.53 - 3.7)	
<b>Total</b>	<b>2319</b>	<b>170 (7.3%)</b>					

\*Deprivation score ranges: most affluent (least deprived) 1-30, intermediate 31-54 and poorest (most deprived) 55-86.

## Discussion

Having a low CD4 count and/or a high viral load has been established to be a risk factor for progression to more serious HIV disease. The aim of this analysis was to establish risk factors for these unfavourable clinical signs. Deprivation is the only demographic variable to significantly predict potential ill-health, regardless of the definition used (be it low CD4 count, detectable or high viral load or a combination of these), and this testifies to the powerful relationship between ill-health and deprivation<sup>11</sup> (see also chapters 4, 8 and 11).

Deprivation was found to be a predictor of:

- o a CD4 count of less than 200;
- o a viral load of 50 copies/ml or more; and
- o a simultaneous CD4 count of less than 200 and viral load of 10,000 or more.

The North West is one of the most deprived English regions. When compared with the national profile, a third of the North West population fall into the most deprived fifth of the population of England as a whole<sup>11</sup>. The HIV positive population is even more skewed towards the poorer areas, with one third of those categorised as 'most affluent' actually residing in the poorest two-fifths of the country, and a further third being intermediate in terms of deprivation on a national level (data not shown). Thus, relatively, people with HIV who are living in the poorest areas of the region are amongst the more deprived populations in the region. We know that poverty has an impact on accessing health care<sup>11,12,13</sup> and has an impact on people living with HIV<sup>14,15</sup>. That deprivation was found to be a predictor of lower CD4 count and higher viral loads is important in the treatment and monitoring of HIV. We have previously shown that those living in the poorest areas of the region are more likely to require a hospital stay than those with HIV living in the most affluent areas<sup>14</sup>. This chapter demonstrates, using a sub sample of the North West HIV positive population (for whom CD4 count and viral load records are available), that a low CD4 count and higher viral load is likely to mediate the relationship between poverty and ill-health. The analysis in this chapter confirms that those who had stayed one or more nights in hospital were more likely to have a low CD4 count and a high viral load. The precise causes of the relationship between poverty and HIV-related ill-health are unknown. It is possible that absolute material disadvantage leads to inadequate housing, poor nutrition and increased exposure to infectious disease and thus worsening health<sup>15</sup>, leading to a weakened immune system. Social factors can play a part in the progression of HIV infection and overall well-being is an important part of the health of people with HIV. CD4 count in particular can be affected by stress<sup>1</sup>. The relationship between deprivation and HIV prevalence, incidence and treatment and care is analysed in more detail in chapter 4.

Age group and ethnicity were not significant predictors of having a low CD4 count, an undetectable viral load, or a low CD4 count and high viral load. It is important to note that whilst ethnicity did not come out as a significant variable in the multivariate analysis, deprivation did. Deprivation and ethnicity are closely related variables (see analysis in chapter 4). At the univariate level, ethnicity and deprivation were significantly related to having a low CD4 count and related to having both a low CD4 count and a higher viral load. Research on virulence markers in Switzerland purposely restricted their analysis to individuals of white ethnicity as their pilot work found that ethnicity had an effect on virulence<sup>16</sup> although it was not stated exactly where the effect lay. Our research suggests that other factors (principally infection route and deprivation) have a stronger effect on CD4 counts and viral load.

Those on ART were more likely to have a low CD4 count. This is likely to be due to current recommendations that ART should be commenced in individuals before their CD4 falls below 200 cells/mm<sup>3</sup> and in any individual with a CD4 count of less than 200 cells/mm<sup>3</sup> at diagnosis<sup>8</sup>. However, those on ART were found to be less likely to have a detectable viral load. The preferable outcome of ART is to reduce the viral load to an undetectable level after 24 weeks<sup>8</sup>. Although these appear to be conflicting findings, these two indicators of health in an HIV positive individual do not correlate perfectly (see table 5.1). Those individuals on ART were found to be more likely to have a CD4 count of less than 200 cells/mm<sup>3</sup> and a viral load of 50 copies/ml or more. This may possibly be due to an aging HIV positive population (who may have a longer-standing infection) as the majority of individuals included in the analysis are not new cases. It is possible that this pattern may change in future years with the introduction of new classes and combinations of ART drugs. The relationship between ART and CD4 count/viral load would, however, be clearer with further analysis. The length of time on ART (a new variable on the dataset for 2006), length of infection and whether an individual has just commenced ART (therefore may have a low CD4 count) or has been on ART for some time (therefore may have an undetectable viral load) are all key to understanding the relationship. However, a further longitudinal study would be required to address these research questions. Due to the uncertainty over the sequence of events, the third analysis sought to identify factors related to being most at risk of progressing to more serious HIV disease, for which those individuals with a simultaneous low CD4 count and a higher viral load were selected. Those on ART were more likely to have a simultaneous low CD4 count and a higher viral load than those not on ART. This suggests that these individuals may have started ART recently in response to a low or falling CD4 count and higher viral load. Nearly 17% of individuals who were new to the treatment and care database in the North West in 2005 (note that these are often, but not necessarily, new diagnoses) were in this most at-risk category (i.e. with a low CD4 count and high viral load: table 5.4). This is important as it suggests that a substantial proportion of those new to treatment have not been detected early enough and may have poorer outcomes.

It was found in chapter 3 that median CD4 count at diagnosis in the North West has remained fairly steady over time, with an overall slight increase from 290 cells/mm<sup>3</sup> up to 2002 to 342 cells/mm<sup>3</sup> in 2005. Median viral load at

diagnosis has fallen from 75,000 copies up to 2002 to 29,300 copies/ml in 2005. Despite this evidence of increasing the rate of early diagnosis, the fact that 17% of those new to the treatment and care database have a high viral load and a CD4 count below 200 cells/mm<sup>3</sup> (table 5.4) suggests that there is considerable scope for improvement.

While these analyses highlight some interesting and potentially important findings, they are limited by being based on only a partial dataset. The importance of monitoring CD4 count and viral load over time in individuals is known<sup>1</sup> but monitoring them together is important both on an individual basis and at a regional level to help to maintain the health of HIV positive people in the region. Studying trends in these markers would enable patterns to be observed in different cohorts on a more local level, which may indicate if treatment is being successful or failing. It is key that CD4 and viral load continue to be reported to the HIV monitoring system and that its completeness from each treatment centre is improved to give a more accurate analysis of the relationships between these disease indicators and factors that influence the health of people living with HIV in the North West of England. The analyses have shown some important relationships, in particular that between ill-health, or potential ill-health, and deprivation. CD4 count and viral load are important fields collected as part of the twice-yearly HIV data collection. CD4 count and viral load have been collected by the North West HIV/AIDS Monitoring Unit at the Centre for Public Health since the end of the 1990s and the quality and completeness has improved year on year, enabling these analyses to be conducted. However, there is still opportunity for further analyses on a more complete dataset and for further improvement.

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