Kirby Institute

AUSTRALIAN HIV OBSERVATIONAL DATABASE ANNUAL REPORT

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CD4 cell responses to combination antiretroviral therapy in patients starting therapy at high CD4 cell counts

Background: Many studies have shown the benefit of combination antiretroviral therapy (cART) to suppress viral replication in patients with low CD4 cell counts, which in turn allows an individual's immune system to recover and protect against AIDS and death. However, minimal data has been published on the effect of cART on persons who commence treatment at higher CD4 cell count levels. We examined CD4 cell responses to combination antiretroviral therapy (cART) in patients enrolled in the Australian HIV Observational Database (AHOD) who commenced cART at CD4 cell counts >350 cells/µL.

Methods: Retrospective and prospective data were examined from HIV positive adults from AHOD who had commenced cART after 1st January 1997 with no prior antiretroviral therapy, and had a baseline CD4 count >350 cells/µL. Assuming "intention-to-treat" principles, CD4 responses were compared according to initial baseline CD4 counts and were modelled using random-effects, repeated-measurement models. Models were adjusted for age, gender, baseline HIV-RNA, recent seroconversion and calendar year. Using published AIDS and/or death incidence rates combined with the data summarised by time and predicted CD4 cell count, we calculated the expected absolute and relative reduction in risk of an event for different starting baseline CD4 strata.

Results: Of the 3,173 AHOD patients recruited, 432 were eligible for the analysis. A total of 4,057 CD4 measurements were observed over a combined total of 1957 patient years. CD4 cell response was largely predicted by time since commencement of cART, baseline CD4 and their interaction. The proportion of patients whose CD4 counts were above 500 cells/µL at 12 months (by baseline CD4 strata 351-500, 501-650 and 650+ cells/µL respectively) was 64%, 84%, 93% and by 72 months was 70%, 69%, 73% **[Figure 1]**. Mean CD4 counts increased above 500 cells/µL in all baseline CD4 strata by 12 months (means of 596, 717 and 881 cells/µL in baseline CD4 strata 351-500, 501-650 and >650 cells/µL respectively). After 72 months since initiating cART, mean CD4 cell counts (by increasing baseline CD4 strata) were 689, 746, 742 cells/µL **[Figure 2]**. The expected relative reduction in risk of AIDS or mortality for baseline CD4 count group >650 cells/µL relative to 351-500 cells/µL group was approximately 14%, or an absolute risk reduction of 1.25 per 1000 treated patient years **[Table 1]**.

Table 1: Cummulative proportion of time (patient-years) predicted for CD4 strata over follow-up (72 months) and the estimated Absolute Risk Reduction and Relative Risk Reduction of AIDS and (or) death incidence.

				AIDS/Death			
Baseline CD4 (cells/µL)	Predicted CD4 strata (cells/µL)	Follow-up (%) in CD4 strata	Hypothetical Patient Year Split (N=1,000)	Estimated No. Events by CD4 strata	Total Estimate No. Events	ARR	RRR
$CD4_{BL}$ 351-500	<500	18	180	2.3			
	501-650	40	398	3.6	8.9	0	1
	650+	42	422	3			
$CD4_{BL}$ 501-650	<500	11	113	1.5			
	501-650	27	269	2.4	8.2	-0.66	0.93
	650+	62	618	4.3			
$CD4_{BL}$ >650	<500	4	41	0.5			
	501-650	19	190	1.7	7.6	-1.25	0.86
	650+	77	770	5.4			

Conclusion: Patients starting cART at high CD4 cell counts (>650 cells/µL) tend to maintain this immunological level over six years of follow-up. Patients starting from 351-500 CD4 cells/µL achieve levels of >650 cells/µL after approximately three years of cART. Initiating cART with a baseline CD4 count 501-650 or >650 cells/µL relative to 351-500 cells/µL indicated a minimal reduction in risk of AIDS incidence and/or death.

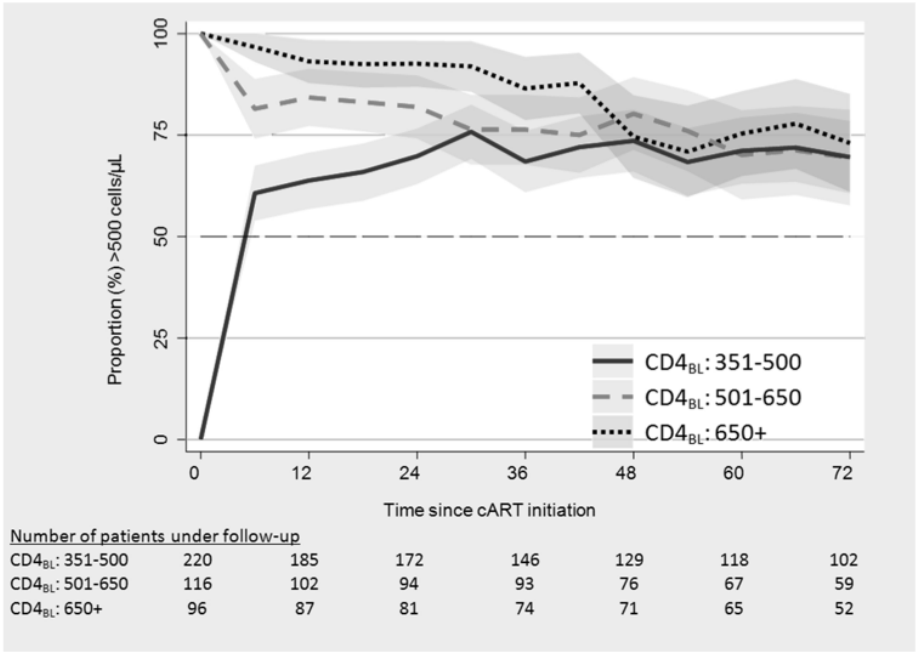


FIGURE 1. The proportion of patients with CD4 count >500 cells per microliter over time since initiation of cART. The shaded regions represent a 95% binomial proportion confidence interval.

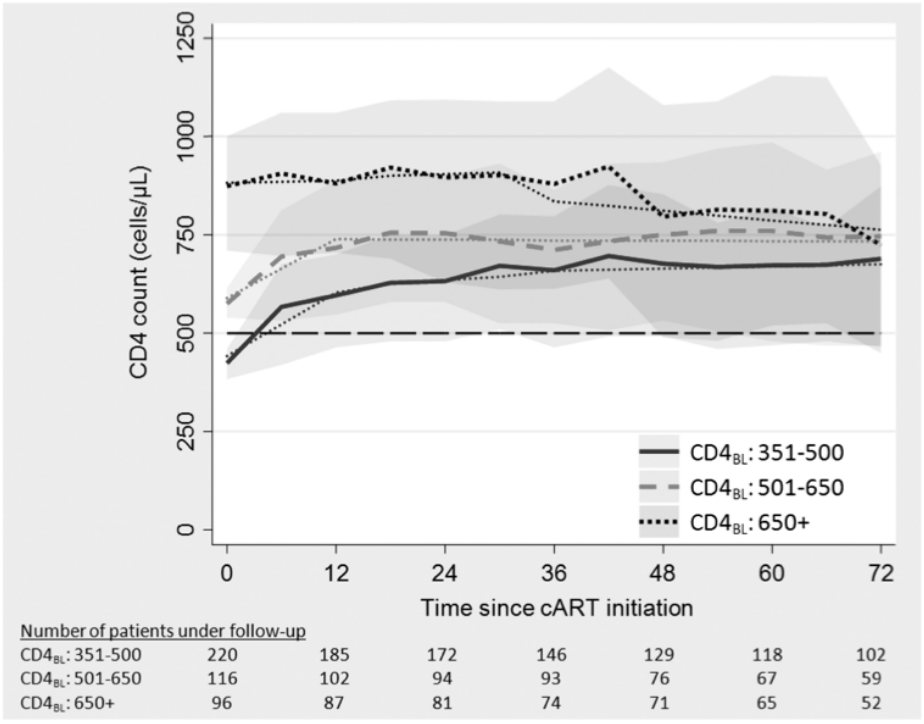


FIGURE 2. Mean CD4 cell count (modeled—dots) over time since initiating cART, stratified by baseline CD4 count. Shaded bands are the interquartile range for the observed CD4 cell counts at a given time point.

Reference: Wright ST, Carr A, Woolley I, Giles M, Hoy J, Cooper DA, et al. CD4 cell responses to combination antiretroviral therapy in patients starting therapy at high CD4 cell counts. J Acquired Immune Deficency Syndromes (2011); 58:72–79.

Table 1: All AHOD demographics[1] (Total – 3 572)

	Number	(%)		Number	(%)
Sex			**CD4 (cells/µl)** [1]		
Male	3336	(93)	<200	373	(12)
Female	228	(6)	200-299	1052	(11)
Transgender	8	(0)	300-499	1526	(31)
			500+	503	(46)
Age (years) [1]			Missing	400	
<30	349	(10)	Mean [SD]	*221*	*[280]*
30-39	1306	(37)			
40-49	1176	(33)	**HIV viral load (copies/ml)** [1]		
50+	741	(21)	≤400	1965	(59)
Mean [SD]	*42*	*[10]*	401-10 000	591	(18)
			>10 000	773	(23)
Aboriginal/Torres Strait islander[2]			Missing	243	
Yes	41	(1)	Median [LQ – UQ][4]	*400*	*[400-8000]*
No	2187	(61)			
Missing	1344	(38)	**Prior AIDS defining illness**[1]		
			Yes	608	(17)
Exposure category			No	2964	(83)
Male homosexual contact	2616	(73)			
Male homosexual contact and IDU	129	(4)	**Hepatitis C ever**		
Injecting drug user (IDU)	74	(2)	Yes	384	(11)
Heterosexual contact	367	(10)	No	3188	(89)
Receipt of blood/blood products	21	(1)			
Other	307	(9)	**Hepatitis B ever**		
Missing	58	(2)	Yes	151	(4)
			No	3421	(96)
Estimated year of HIV infection[3]					
<1985	10	(0)	**Total patients under active follow up in last 12 months (N=2022)**[5]		
1985-1989	112	(3)			
1990-1994	353	(10)			
1995+	755	(21)	**Recent CD4 (cells/µl)** [6]		
Missing	2342	(66)	< 200	87	(5)
			200-299	103	(5)
Metropolitan/non-metropolitan clinic			300-499	491	(26)
Metropolitan	2945	(82)	500+	1221	(64)
Non-metropolitan	627	(18)	Missing	120	
			Mean [SD]	*624*	*[293]*
Region of birth					
Australia and New Zealand	1818	(51)	**Recent HIV viral load (copies/ml)** [6]		
Asia and Oceania	157	(4)	≤400	1647	(90)
Britain and Ireland	120	(3)	401-10 000	73	(4)
Europe	91	(3)	>10 000	106	(6)
Africa and Middle East	55	(2)	Missing	196	
North America	27	(1)	Median [LQ – UQ][4]	*400*	*[400-400]*
South America	28	(1)			
Missing	1276	(36)			

1. Age & prior AIDS defining illness at time of cohort enrolment. CD4 count & HIV viral load closest to and within 3 months of cohort enrolment date.
2. Data not available for 8 of 28 sites
3. Year of HIV infection = mid date between date of first positive and last negative test (coded as missing if either first positive or last negative date are missing).
4. LQ = Lower quartile UQ = Upper quartile.
5. Most recent visit is between March 31, 2011 and March 31, 2012
6. Most recent CD4 count & HIV viral load between March 31, 2011 and March 31, 2012

Table 2: Follow up status by calendar year

Year	Entered study	Deaths	Lost to Follow up
1999[1]	817	6	37
2000	861	25	49
2001	248	29	65
2002	164	23	68
2003	197	22	59
2004	85	19	84
2005	98	26	70
2006	121	28	68
2007	97	25	94
2008	88	22	124
2009	305	16	98
2010	240	21	124
2011	133	17	51
2012[2]	118	3	0
Total	**3572**		

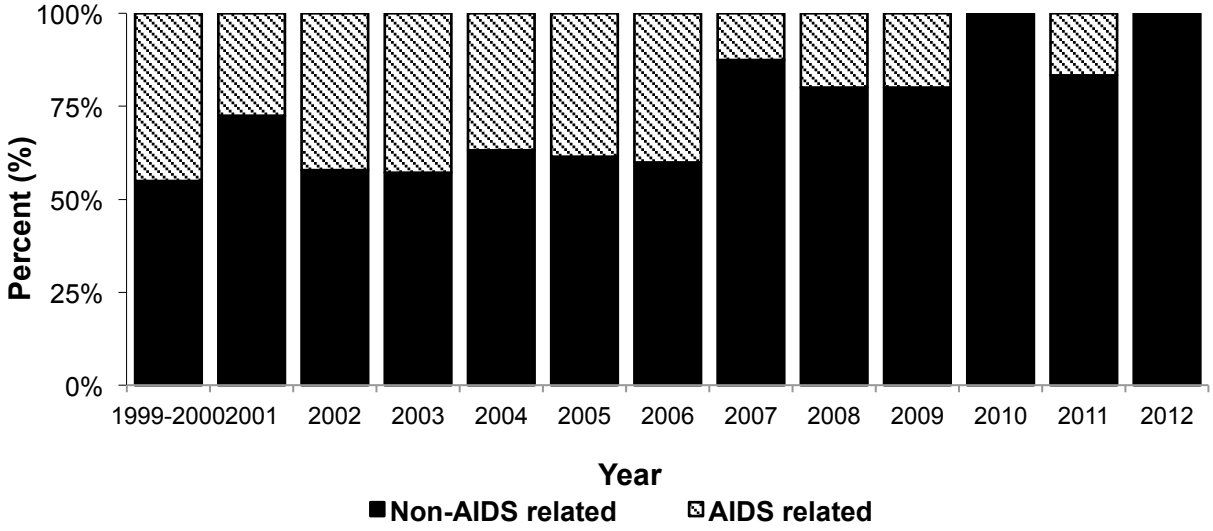
Complete follow-up (percentage of patients)[3]: 72%

Loss to follow-up (per 100 person years): 4.15 (95% CI: 3.89-4.43)

Mortality (per 100 person years): 1.27 (95% CI: 1.13-1.43)

1. July 1 - December 31, 1999.
2. January 1 - March 31, 2012.
3. Patients who have died or any patients seen at clinic site within the last 12 months (March31, 2011 - March 31, 2012) are considered to have complete follow-up.

Figure 1: Proportion of AIDS and non-AIDS related deaths in AHOD since cohort enrolment by year[1]



[1]2012 data omitted due to a low number of observations (N=3) over the period 1 January – 31 March 2012.

Table 3: Total number of deaths in AHOD since cohort enrolment, by AIDS or non-AIDS related classification and year

	1999-2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012[1]	All years
Non-AIDS related	17	21	11	12	12	16	15	21	16	8	11	5	2	**167**
AIDS related	14	8	8	9	7	10	10	3	4	2	0	1	0	**76**
Unknown	0	0	4	1	0	0	3	1	2	6	8	7	1	**33**
Total deaths	**31**	**29**	**23**	**22**	**19**	**26**	**28**	**25**	**22**	**16**	**19**	**13**	**3**	**276**

[1]1 January –31 March 2012

Table 4: Summary of AIDS defining illness and non-AIDS related deaths reported since cohort enrolment and within the last year[1]

Type of AIDS defining illness	N=12	Non-HIV related deaths	N=6
HIV encephalopathy	2	Cancer	2
Kaposi's Sarcoma	2	Renal Failure	2
Pneumocystis carinii/jirovecii pnuemonia	2	CVD	1
HIV wasting syndrome	2	Suicide	1
Candidiasis of the bronchi, trachea or lungs	1		
Oesophageal candidiasis	1		
Coccidiodomycosis	1		
Toxoplasmosis	1		

[1]31 March 2011 – 31 March 2012

Table 5: Trends in antiretroviral treatment[1]

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012[2]
Patients under active follow up[1]	(N=1563)	(N=1718)	(N=1790)	(N=1906)	(N=1887)	(N=1892)	(N=1915)	(N=1893)	(N=1756)	(N=1907)	(N=1829)	(N=1520)
Treatment	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)
Never treatment	181 (12)	181 (11)	179 (10)	183 (10)	166 (9)	161 (9)	154 (8)	161 (9)	137 (8)	128 (7)	115 (6)	83 (5)
Ever treatment	**N=1382**	**N=1537**	**N=1611**	**N=1723**	**N=1721**	**N=1731**	**N=1761**	**N=1732**	**N=1619**	**N=1779**	**N=1714**	**N=1437**
Currently[3]	1168 (75)	1252 (73)	1284 (72)	1410 (74)	1437 (76)	1499 (79)	1580 (83)	1572 (83)	1511 (86)	1699 (89)	1651 (90)	1401 (92)
Previously, not currently	214 (14)	285 (17)	327 (18)	313 (16)	284 (15)	232 (12)	181 (9)	160 (8)	108 (6)	80 (4)	63 (3)	36 (2)
Number of drugs ever[4]												
≤3	321 (23)	293 (19)	284 (18)	290 (17)	267 (16)	263 (15)	266 (15)	249 (14)	249 (15)	370 (21)	414 (24)	380 (26)
4-6	485 (35)	556 (36)	539 (33)	549 (32)	520 (30)	471 (27)	448 (25)	438 (25)	389 (24)	417 (23)	402 (23)	325 (23)
7-9	365 (26)	407 (26)	436 (27)	475 (28)	483 (28)	499 (29)	482 (27)	468 (27)	413 (26)	391 (22)	349 (20)	282 (20)
10+	211 (15)	281 (18)	352 (22)	409 (24)	451 (26)	498 (29)	565 (32)	577 (33)	568 (35)	601 (34)	549 (32)	450 (31)
Number of drug classes ever[4]												
1	67 (5)	65 (4)	70 (4)	62 (4)	47 (3)	44 (3)	42 (2)	35 (2)	28 (2)	32 (2)	45 (3)	35 (2)
2	642 (46)	662 (43)	650 (40)	660 (38)	616 (36)	591 (34)	612 (35)	609 (35)	582 (36)	677 (38)	658 (38)	568 (40)
3	672 (49)	795 (52)	871 (54)	970 (56)	1015 (59)	1042 (60)	1041 (59)	1003 (58)	862 (53)	825 (46)	728 (42)	563 (39)
4	-	14 (1)	19 (1)	30 (2)	42 (2)	49 (3)	57 (3)	63 (4)	108 (7)	177 (10)	211 (12)	209 (15)
5	-	-	-	-	-	5 (0)	9 (1)	21 (1)	34 (2)	62 (3)	65 (4)	56 (4)
6	-	-	-	-	-	-	-	1 (0)	5 (0)	6 (0)	7 (0)	6 (0)

1. Treatment status for all patients under active follow up to the 1st January of each year is included in this analysis. Includes prospective data only (i.e. records prior to AHOD enrolment are excluded).
2. 1st January-31st March 2012
3. Currently on treatment is defined as receiving treatment to the 1st January of each year.
4. Denominator is the number of patients who have ever received treatment.

Table 6: Trends in combination antiretroviral treatment[1]

	2001		2002		2003		2004		2005		2006		2007		2008		2009		2010		2011		2012[2]	
Combination[3]	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
1st combination	381	(25)	337	(21)	333	(20)	346	(21)	299	(18)	285	(17)	295	(17)	331	(19)	408	(25)	378	(23)	371	(26)	277	(26)
2nd combination	283	(18)	266	(17)	256	(16)	259	(15)	238	(14)	246	(14)	278	(16)	299	(17)	301	(18)	341	(21)	327	(23)	244	(23)
3rd combination	168	(11)	173	(11)	194	(12)	206	(12)	211	(12)	226	(13)	203	(12)	210	(12)	203	(12)	224	(14)	194	(13)	158	(15)
4th + combination	174	(11)	242	(15)	275	(17)	321	(19)	362	(21)	443	(26)	501	(29)	524	(30)	505	(31)	507	(31)	442	(31)	335	(31)

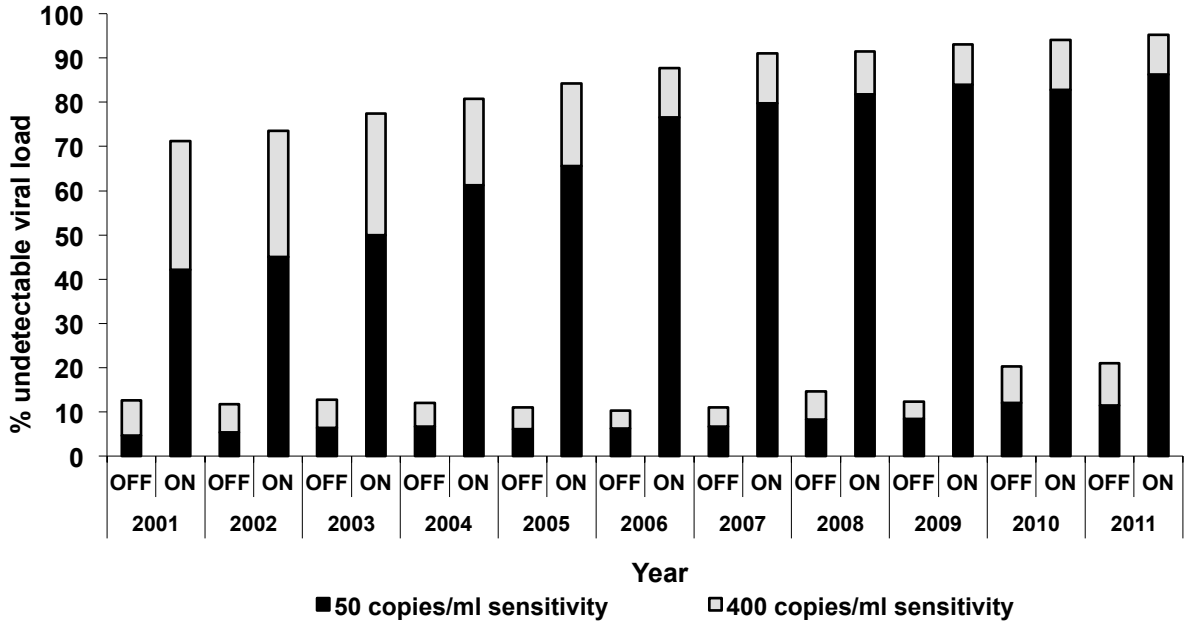
1. Patients are classified according to their combination anti retroviral therapy (ART) with the longest duration in each calendar year. Includes patients who commenced their first combination ART after January 1, 1997 for at least 14 days. The denominator includes all AHOD patients that could have been on antiretroviral treatment in any calendar year (i.e. HIV positive), who commenced their first combination ART after January 1, 1997 for at least 14 days, or were only on mono/dual therapy, or never received any treatment.Includes prospective and retrospective data.
2. 31 March 2011 – 31 March 2012.
3. Combinations include 3 or more antiretroviral drugs, does not include mono/dual therapy. Regimens with interruptions of less than 7 days were considered as continuous treatment.

Table 7: Immunological and virological trends[1]

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Viral load (copies/ml)											
Total N (with measure)	2042	2071	2052	2062	2110	2103	2155	2197	2057	1932	1834
Off Treatment[2]											
No. with a viral load count[4]	415	450	469	433	465	399	390	350	275	207	167
Median	20800	20500	18800	21900	18300	14750	13593	12130	10882	9173	6830
IQR	4100-64500	3990-65300	3680-64550	4370-69300	3850-63100	4000-52000	3100-40500	2400-36500	2100-34900	790-33900	543-42600
On Treatment[3]											
No. with a viral load count[4]	1627	1621	1583	1629	1645	1704	1765	1847	1782	1725	1667
Median	224.5	135	51	50	50	50	50	50	50	50	50
IQR	50-685	50-460	50-399	50-365	50-225	50-50	50-50	50-50	50-50	50-50	50-50
CD4 count (cells/µl)											
Total N (with measure)	2050	2088	2070	2078	2116	2093	2155	2192	2098	1982	1905
Off Treatment[2]											
No. with a CD4 count[5]	416	459	475	444	471	402	391	349	272	209	167
Median	506	500	490	493	500	510	504	499	520	502	529
IQR	370-685	365-659	364-655	378-655	377-668	394-684	404-650	390-668	408-687	400-670	409-681
On Treatment[3]											
No. with a CD4 count[5]	1634	1629	1595	1634	1645	1691	1764	1843	1826	1773	1738
Median	510	512	507	500	501	520	530	540	555	564	590
IQR	325-722	325-727	330-710	335-702	340-705	360-717	370-730	390-750	400-740	408-746	439-780

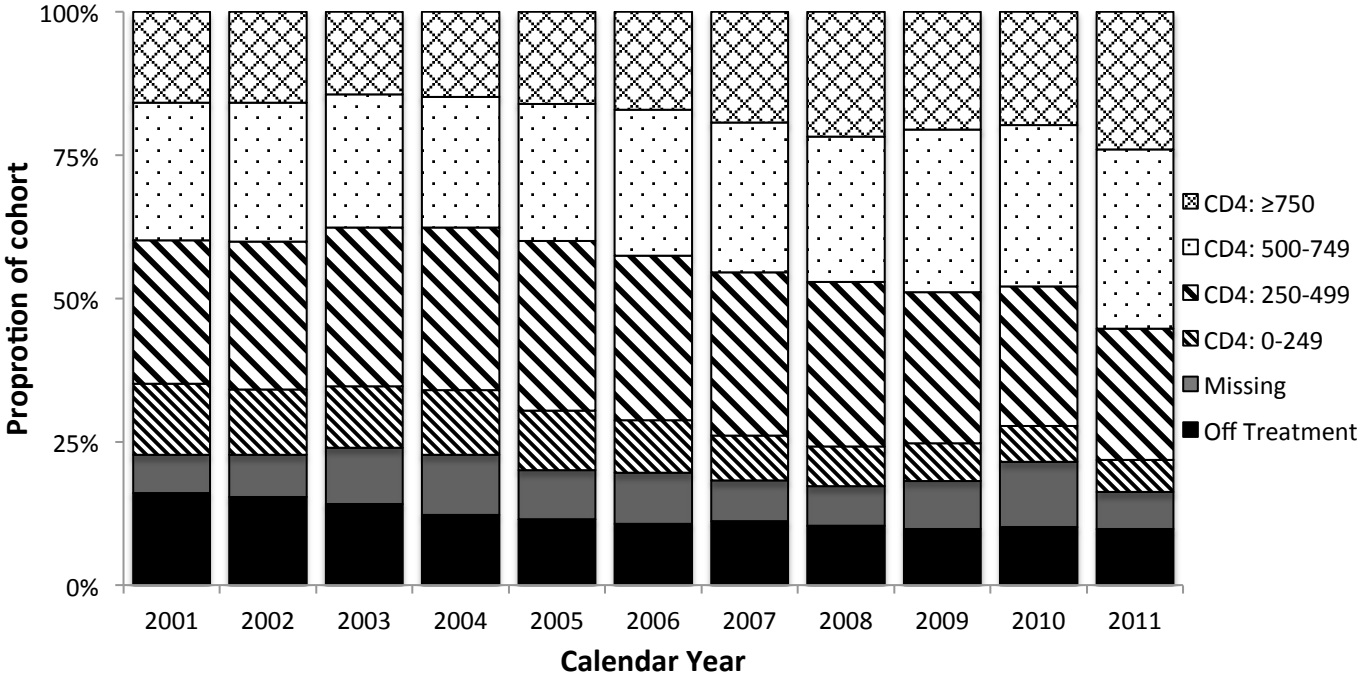
1. Includes retrospective and prospective data. Off treatment if never on a regimen of duration greater than 14 days for given calendar year. Viral load taken as median value during regimen of longest duration for given calendar year. Undetectable assay level taken as ≤50 copies/ml. Data for 2000 and 2001 includes 2 sites with minimum assay sensitivity of 400 copies/ml. Data for 2002 includes 1 site with minimum assay sensitivity of 400 copies/ml
2. Patients who have not received treatment during the calendar year
3. Patients who have received any treatment during the calendar year
4. Includes patients with a viral load measured during the relevant calendar year.
5. Includes patients with a CD4 count measured during the relevant calendar year

Figure 2: Proportion of patients with an undetectable viral load, by treatment status (off /on treatment) and year according to assay sensitivity[1]



1. Off treatment if never on a regimen of duration greater than 14 days for given calendar year. Viral load taken as median value during regimen of longest duration for given calendar year. Data for 2000 and 2001 includes 2 sites with minimum assay sensitivity of 400 copies/ml. Data for 2002 includes 1 site with minimum assay sensitivity of 400 copies/ml

Figure 3: CD4 cell counts (cells/µl) in patients receiving treatment by calendar year[1-3].



1. Includes patients with a prospective CD4 measure during the relevant calendar year.
2. For patients on treatment, analysis based on the initial treatment intent, not on treatment administered (ITT), i.e. no adjustments are made for off-treatment following cART initiation.
3. Patients off treatment include those who have enrolled and have not intiated combination antiretroviral therapy.

Table 8: Top ten treatment combinations among the AHOD cohort[1]: January-December 2011

In 2011, there were a total of 397 unique antiretroviral treatment (ART) combinations among the 1867 AHOD patients on combination ART. A total of 2115 combination regimens were recorded among these patients throughout 2011. The top ten most common ART combinations are described below.

ART combinations	Number of regimens recorded during 2011
emtricitabine + efavirenz + tenofovir	364
emtricitabine + nevirapine + tenofovir	161
abacavir + lamivudine + nevirapine	153
emtricitabine + atazanavir + ritonavir + tenofovir	153
emtricitabine + tenofovir + raltegravir	76
abacavir + lamivudine + efavirenz	73
abacavir + lamivudine + atazanavir + ritonavir	52
emtricitabine + kaletra + tenofovir	47
lamivudine + zidovudine + nevirapine	44
emtricitabine + ritonavir + tenofovir	29

1. Includes retrospective and prospective data. Combinations include 3 or more antiretroviral drugs. Fixed dose combinations are separated into individual component antiretroviral drugs.

Table 9: Current use of individual antiretroviral treatments[1]

	2002		2003		2004		2005		2006		2007		2008		2009		2010		2011		2012[8]	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Nucleoside analogue reverse transcriptase inhibitors (RTI)																						
Abacavir	541	(21)	515	(20)	531	(21)	504	(20)	436	(17)	343	(14)	332	(13)	232	(10)	213	(9)	183	(9)	118	(8)
Combivir[2]	358	(14)	332	(13)	375	(15)	370	(15)	330	(13)	236	(9)	182	(7)	147	(6)	135	(6)	98	(5)	66	(4)
Didanosine	432	(17)	394	(16)	350	(14)	269	(11)	192	(8)	123	(5)	91	(4)	57	(2)	46	(2)	25	(1)	17	(1)
Emtricitabine	1	(0)	1	(0)	1	(0)	38	(1)	94	(4)	63	(2)	89	(4)	89	(4)	102	(4)	101	(5)	76	(5)
Kivexa[3]	6	(0)	7	(0)	15	(1)	93	(4)	311	(12)	409	(16)	440	(18)	412	(17)	370	(16)	326	(16)	244	(16)
Lamivudine	968	(38)	931	(37)	963	(38)	957	(38)	859	(34)	544	(21)	466	(19)	338	(14)	296	(13)	242	(12)	163	(10)
Stavudine	609	(24)	423	(17)	275	(11)	178	(7)	115	(5)	71	(3)	56	(2)	40	(2)	28	(1)	13	(1)	8	(1)
Tenofovir	252	(10)	502	(20)	602	(24)	729	(29)	758	(30)	492	(19)	435	(17)	374	(16)	343	(15)	282	(14)	198	(13)
Trizivir[4]	140	(6)	151	(6)	144	(6)	138	(5)	122	(5)	87	(3)	67	(3)	54	(2)	41	(2)	30	(1)	17	(1)
Truvada[5]	5	(0)	7	(0)	8	(0)	15	(1)	363	(14)	535	(21)	689	(27)	856	(36)	863	(37)	650	(31)	464	(30)
Zalcitabine	24	(1)	15	(1)	10	(0)	8	(0)	5	(0)	4	(0)	4	(0)	3	(0)	2	(0)	2	(0)	2	(0)
Zidovudine	292	(12)	257	(10)	247	(10)	200	(8)	162	(6)	121	(5)	97	(4)	56	(2)	44	(2)	25	(1)	19	(1)
Apricitabine	-		-		-		1	(0)	1	(0)	1	(0)	1	(0)	1	(0)	1	(0)	-		-	
Non-nucleoside analogue RTI																						
Delavirdine	19	(1)	18	(1)	18	(1)	12	(0)	12	(0)	10	(0)	4	(0)	3	(0)	3	(0)	1	(0)	1	(0)
Efavirenz	383	(15)	416	(16)	451	(18)	434	(17)	459	(18)	485	(19)	491	(20)	488	(20)	428	(18)	226	(11)	160	(10)
Nevirapine	664	(26)	652	(26)	649	(25)	615	(24)	598	(24)	607	(24)	620	(25)	581	(24)	536	(23)	455	(22)	316	(20)
Etravirine	-		-		-		-		3	(0)	23	(1)	47	(2)	73	(3)	85	(4)	83	(4)	64	(4)

1. All treatment records of ≥2 weeks of treatment in any calendar year were included in this analysis. The denominator includes all patients that could have been on antiretroviral therapy (i.e. HIV positive) in any calendar year. The proportion of patients on each drug in any calendar year does not add up to 100% across all ART drug groups in each calendar year as patients on more than one ARV during a calendar year period will be counted in all of the relevant ART groups. Includes retrospective and prospective data.
2. Comibivir – Lamivudine & Zidovudine.
3. Kivexa – abacavir & lamivudine.
4. Trizivir - abacavir & lamivudine & zidovudine.
5. Truvada – tenofovir & emtricitabine;
6. Kaletra – lopinavir & ritonavir;
7. Atripla – tenofovir & emtricitabine & efavirenz.
8. 1st January-31st March.

Table 9 continued: Current use of individual antiretroviral treatments[1]

	2002		2003		2004		2005		2006		2007		2008		2009		2010		2011		2012[8]	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Protease Inhibitor																						
Amprenavir	72	(3)	61	(2)	46	(2)	40	(2)	31	(1)	28	(1)	28	(1)	29	(1)	27	(1)	23	(1)	15	(1)
Atazanavir	4	(0)	135	(5)	256	(10)	375	(15)	431	(17)	459	(18)	505	(20)	495	(21)	482	(21)	420	(20)	301	(19)
Darunavir	-		-		6	(0)	11	(0)	40	(2)	72	(3)	116	(5)	157	(7)	185	(8)	194	(9)	146	(9)
Fosamprenavir	2	(0)	1	(0)	2	(0)	32	(1)	37	(1)	33	(1)	30	(1)	24	(1)	16	(1)	12	(1)	7	(0)
Indinavir	249	(10)	170	(7)	114	(4)	63	(2)	40	(2)	27	(1)	19	(1)	9	(0)	6	(0)	4	(0)	4	(0)
Kaletra[6]	305	(12)	367	(14)	383	(15)	382	(15)	363	(14)	343	(14)	307	(12)	281	(12)	271	(12)	204	(10)	143	(9)
Nelfinavir	175	(7)	127	(5)	96	(4)	61	(2)	41	(2)	28	(1)	8	(0)	6	(0)	4	(0)	3	(0)	1	(0)
Ritonavir	350	(14)	378	(15)	456	(18)	538	(21)	607	(24)	629	(25)	679	(27)	657	(28)	652	(28)	611	(30)	452	(29)
Saquinavir	169	(7)	142	(6)	121	(5)	110	(4)	91	(4)	74	(3)	60	(2)	41	(2)	31	(1)	27	(1)	18	(1)
Tipranavir	1	(0)	11	(0)	16	(1)	22	(1)	18	(1)	9	(0)	7	(0)	5	(0)	3	(0)	3	(0)	0	(0)
Fusion Inhibitor																						
Enfurvitide	28	(1)	45	(2)	53	(2)	59	(2)	64	(3)	56	(2)	45	(2)	35	(1)	28	(1)	20	(1)	13	(1)
CCR5																						
Maraviroc	-		-		-		8	(0)	7	(0)	6	(0)	14	(1)	21	(1)	28	(1)	31	(2)	24	(2)
Integrase Inhibitors																						
Raltegravir	-		-		-		-		11	(0)	65	(3)	173	(7)	291	(12)	410	(18)	417	(20)	331	(21)
Class Combinations																						
Atripla[7]	-		-		-		-		-		-		1	(0)	9	(0)	234	(10)	283	(14)	220	(14)

1. All treatment records of ≥2 weeks of treatment in any calendar year were included in this analysis. The denominator includes all patients that could have been on antiretroviral treatment (i.e. HIV positive) in any calendar year. The proportion of patients on each drug in any calendar year does not add up to 100% across all ARV drug groups in each calendar year as patients on more than one ART during a calendar year period will be counted in all of the relevant ART groups. Includes retrospective and prospective data.
2. Comibivir – Lamivudine & Zidovudine.
3. Kivexa – abacavir & lamivudine.
4. Trizivir - abacavir & lamivudine & zidovudine.
5. Truvada – tenofovir & emtricitabine.
6. Kaletra – lopinavir & ritonavir.
7. Atripla – tenofovir & emtricitabine & efavirenz.
8. 1st January-31st March.

MONITORING DISPENSED ANTIRETROVIRALS VIA THE s100 PROGRAM

Data on the number of patients who were dispensed antiretroviral (ARV) drugs per state per financial year quarter, reported in the Public Hospital Dispensed National Patient Report from the Australian Government's Highly Specialised Drugs (HSD) (s100) program were analysed together with data on ART use from the AHOD sample to estimate total numbers of patients on ART by state and nationally, by year. At this time, all ARV drugs in Australia are publicly funded through the s100 program and should be recorded in the Public Hospital Dispensed National Patient Report. Since patients with HIV infection generally receive three or more ARV drugs in combination, and because the s100 program only collects data on individual ARV drugs, it is not possible to enumerate directly the number of patients receiving ART from the s100 data.

One of the commonly used ARV drugs for treatment of HIV infection is lamivudine. Yet, it is also used for the treatment of hepatitis B infection. As the PBS code is not included in the Public Hospital Dispensed National Patient Report, it is not possible to separate the number of patients who were dispensed lamivudine treatment for HIV from those receiving lamivudine for HBV. Therefore, we estimated the number of person years of lamivudine (100mg tablets) for HBV treatment from the Public Hospital Dispensed National Pack Number Report, which includes the PBS code, dosage and the total numbers of packs dispensed for each drug per financial quarter. To estimate the total number of patients dispensed lamivudine for HIV treatment, we deducted the total number of person years of lamivudine treatment for HBV each year from the total number of patients dispensed lamivudine for HIV and HBV treatment. This method is based on the assumption that the majority of patients received a complete year of treatment during any calendar year period.

To estimate the number of patients receiving ART, we combined data on the proportion of patients receiving certain mutually exclusive ARVs in AHOD with data from the s100 program on the total number of people receiving the same ARVs. For example, lamivudine and emtricitabine are a common component of combination ART regimens in Australia, but should not be prescribed in combination. We calculated the proportion of all treated patients in AHOD who received lamivudine or emtricitabine as part of an ART regimen by year and state. We also estimated the total number of patients dispensed lamivudine or emtricitabine for HIV infection each year through the s100 program by calculating the average number of patients prescribed each drug from the corresponding four financial year quarters. An estimate of the total number of people receiving any ART was then obtained by dividing the total number of patients receiving lamivudine or emtricitabine through the s100 program by the proportion of treated patients in AHOD receiving the same ARV drugs. As a sensitivity analysis, we repeated this calculation for other commonly mutually exclusive drugs, including: 1) efavirenz and nevirapine; 2) Kaletra (lopinavir and ritonavir) and ritonavir; and 3) stavudine and zidovudine containing ARVs. In this report, we have only included results for the lamivudine and emtricitabine model.

Important Note: Prior to 2009, the HSD Report provided prescribed patient numbers by each antiretroviral agent. However after noting some inconsistencies with their methodology, they have since ceased providing these numbers. For years 2009-2010, instead we (The Kirby Institute) evaluated patient numbers by using a combination of total packs dispensed and an average "packs-per-patient" adjustment ratio. The packs-per-patient adjustment figure was calculated from 2008 data, where total packs dispensed and patient numbers were available. However, due to the relatively recent diversification of pack sizes, newer dosing schedules and the introduction of antiretroviral agents that were absent in 2008, we are uncertain as to how our packs-per-patient adjustment ratio has changed over time. Therefore we have opted not to report 2011 data for Table 10. We are working with the producers of the HSD Report to amend these issues and are currently revisiting our methodology for these figures.

Table 10: Number of people dispensed antiretroviral treatment through the Highly Specialised Drugs (s100) program by year and antiretroviral agent

	Year of prescription[1,2]						
Antiretroviral agent	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
Nucleoside analogue reverse transcriptase inhibitors							
Abacavir	1,542	1,592	830	617	586	519	501
Didanosine	1,203	873	601	600	311	207	152
Emtricitabine	-	238	163	28	74	54	76
Lamivudine	3,219	3,641	2,094	697	848	433	641
Stavudine	979	603	346	208	140	96	69
Zalcitabine	21	13	4	0	0	0	0
Zidovudine	385	241	206	189	195	151	150
Lamivudine & Zidovudine	1,989	1,959	1,525	1,527	965	835	662
Abacavir & Lamivudine	-	212	1,592	2,310	2,608	2,681	2,593
Abacavir, Lamivudine & Zidovudine	643	544	431	368	275	241	162
Tenofovir	2,273	3,076	2,504	1,619	1,381	1,232	1,334
Tenofovir & Emtricitabine	-	-	1,671	3,116	4,131	5,369	4,262
Non-nucleoside analogue reverse transcriptase inhibitors							
Delavirdine	32	20	16	11	5	6	6
Efavirenz	1,656	1,896	2,208	2,413	2,704	2,971	2,079
Nevirapine	2,412	2,697	2,387	2,436	2,629	2,701	2,655
Protease inhibitors							
Amprenavir	98	39	17	7	0	0	0
Atazanavir	590	1,207	1,746	2,034	2,229	2,582	2,603
Darunavir	-	-	-	69	369	569	596
Fosamprenavir	3	119	194	188	226	217	155
Indinavir	341	228	144	106	75	48	20
Lopinavir & ritonavir	1,580	1,543	1,543	1,689	1,737	1,536	1,495
Nelfinavir	349	230	136	95	0	0	0
Ritonavir	879	1,330	1,845	2,071	2,393	3,015	3,217
Saquinavir	388	294	226	206	167	142	90
Tipranavir	-	-	-	36	30	28	19
Fusion inhibitors							
Enfuvirtide	54	172	197	191	112	55	32
Integrase inhibitor							
Raltegravir	-	-	-	-	304	931	1,090
Combination Class Agents							
Tenofovir, Emtricitabine & Efavirenz	-	-	-	-	-	-	1,548
Total patients[3]	**7,598**	**8,453**	**9,463**	**9,933**	**10,596**	**11,120**	**11,523**
Total cost[4] ($'000s)	**85,293**	**98,485**	**110,512**	**118,847**	**135,532**	**155,556**	**182,888**

1. The number of people dispensed each antiretroviral drug during a calendar year was estimated by calculating the average of the total number of people dispensed each drug during the corresponding financial year quarters. Number of person years for July - December 2009 onwards estimated from the HSD Program Public Hospital Dispensed National Pack Number Report because of changes to S100 data collection methodology.

2 Dashes (-) indicate that data were not available. Person years of Etravirine omitted because of insufficient data.

3. Total patients calculated as (Lamivudine + Combivir (Lamivudine & Zidovudine)+Trizivir (Abacavir, Lamivudine & Zidovudine)+Kivexa (Abacavir & Lamivudine)+Emtricitabine +Truvada(Tenofovir & Emtricitabine))/the proportion of patients in the Australian HIV Observational Database receiving any of the previously mentioned drugs in each year + the estimated number of patients dispensed with combination class agents.

4. Public Hospital Expenditure.

Source: Highly Specialised Drugs (S100) Program

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