AUSTRALIAN HIV OBSERVATIONAL DATABASE ANNUAL REPORT

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Recent Trends in Response to Combination Antiretroviral Therapy in Australia

Background: There have been incremental improvements in combination antiretroviral therapy (cART) over the last 15 years, including increased potency, reduced pill burden, and new drug classes. The aim of this analysis was to assess whether improvements in cART have resulted in improvements in surrogates of HIV outcome.

Methods: Trends in surrogates of treatment outcome for up to four years after treatment commencement were compared by era of treatment commencement: <1996 mono/dual therapy (Mono/Duo); 1996-99 cART; 2000-03 cART; 2004-07 cART; and 2008-13 cART. Changes in CD4 cell count (CD4+) and changes in population proportion with detectable viral load (VL) (>400 copies/ml) following treatment commencement were compared across different eras. Rates of first switch of treatment (≥2 new drugs and/or a new class) were also compared by era.

Results: 2,753 patients were included in the analysis. Patients were predominantly male (94%) and MSM (75%). Mean age increased by later era – **Table 1**.There were differences by era (excluding mono/duo era) in baseline CD4+ ($p<0.001$) and $\log_{10}$VL ($p<0.001$). The proportion of patients with undetectable VL more rapidly reached lower thresholds by later cART era of initiation ($p<0.001$) – **Figure 1A**. CD4+ response was different by later cART era ($p<0.001$), although 1996-99 response was greater than that for 2000-03 ($p=0.007$) – **Figure 1B**.

Probability of switch decreased by later cART era for all switches ($p<0.001$) (**Figure 2A**) and for switches with recent VF ($p<0.001$) (**Figure 2B**) but not for switches without recent VF ($p=0.424$) (**Figure 2C**). Probability of treatment switch after 4 years was 0.58 (95% CI 0.54-0.61) for <1996 mono/duo; 0.53 (0.50-0.57) for 1996-99 cART; 0.44 (0.39-0.50) for 2000-03 cART; 0.39 (0.34-0.45) for 2004-07 cART; and 0.29 (0.25-0.35) for ≥2008 cART.

Conclusion: Across the five time-periods examined, there have been incremental improvements for patients initiated on cART, as measured by overall response of surrogates of HIV outcome (viral load and CD4 count) across treatment eras, and also increased durability of first-line regimens. There were inconsistent changes in clinical stage of initiation which might be explained by evolving attitudes of patients and prescribers to the risk/benefit of cART initiation as the era of cART has unfurled.

Table 1: Patient characteristics at start of treatment by treatment initiation era.

		Pre-cART (<1996)	Early cART (1996-99)	Middle cART (2000-03)	Middle/Late cART (2004-07)	Late cART (2008-12)
Number of Patients		767 (100)	817 (100)	330 (100)	310 (100)	529 (100)
Gender	Female	41(5)	39(5)	21 (6)	26 (8)	42 (8)
	Male	726 (95)	778 (95)	309 (94)	284 (92)	487(92)
Age (years)	mean (SD)	37 (8.9)	38 (9.8)	40 (10.4)	43 (9.9)	42 (10.9)
Mode of HIV	MSM	642 (84)	632 (77)	221 (67)	202 (65)	376 (71)
Exposure	Heterosexual	63 (8)	88 (11)	71 (22)	84 (27)	107 (20)
	IDU	38 (5)	67 (8)	21(6)	14 (5)	22 (4)
	Other	24 (3)	30 (4)	17 (5)	10 (3)	24 (5)
Prior ADI	No	706 (92)	718 (88)	278 (84)	270(87)	491 (93)
	Yes	61 (8)	99 (12)	52 (16)	40 (13)	38 (7)
CD4 cell (cells/µl)	Median (IQR)	294 (190-435)	320 (170-475)	250 (120-420)	250 (170-373)	320 (220-430)
VL ($\log_{10}${copies/ml})	Median (IQR)	5.16 (4.61-5.71)	4.89 (4.28-5.43)	5.00 (4.60-5.51)	4.99 (4.26-5.35)	4.78 (4.13-5.04)

Figure 1: Surrogates of HIV outcome in response to treatment over 4 years. [A] Proportion of population with detectable VL. [B] Median change in CD4 cell count.

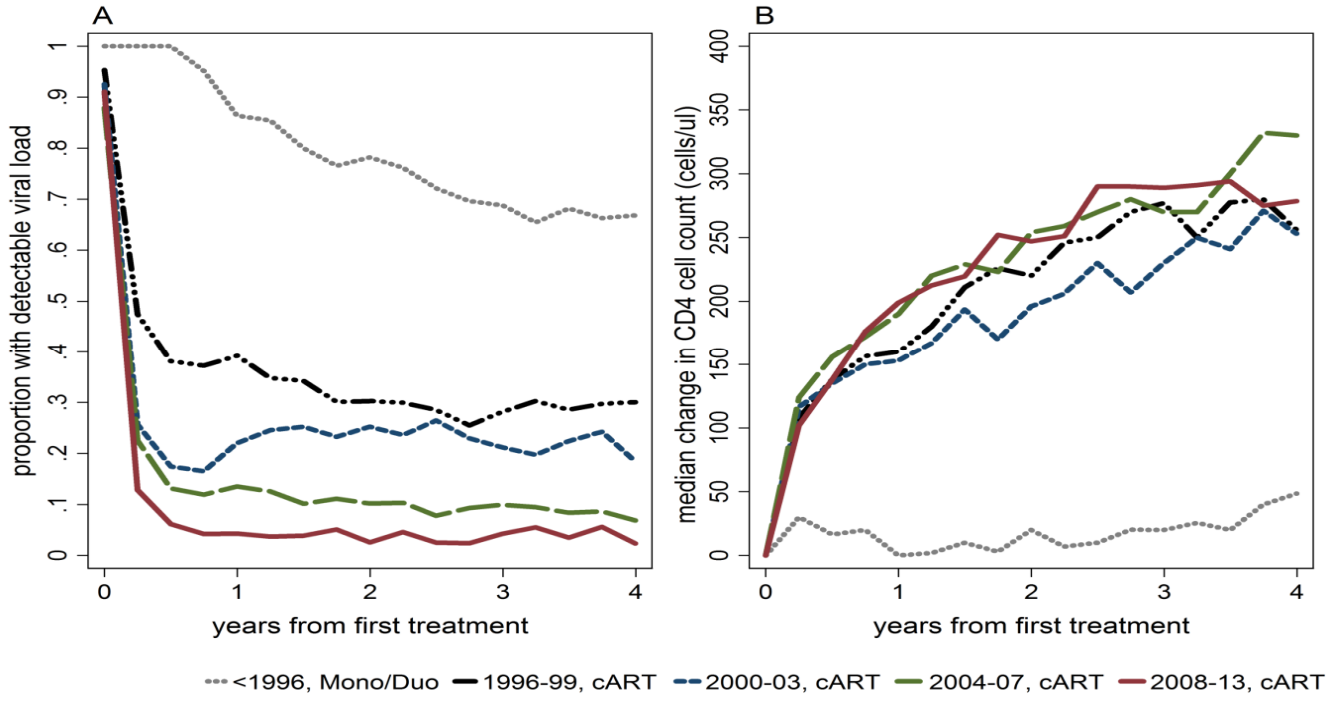
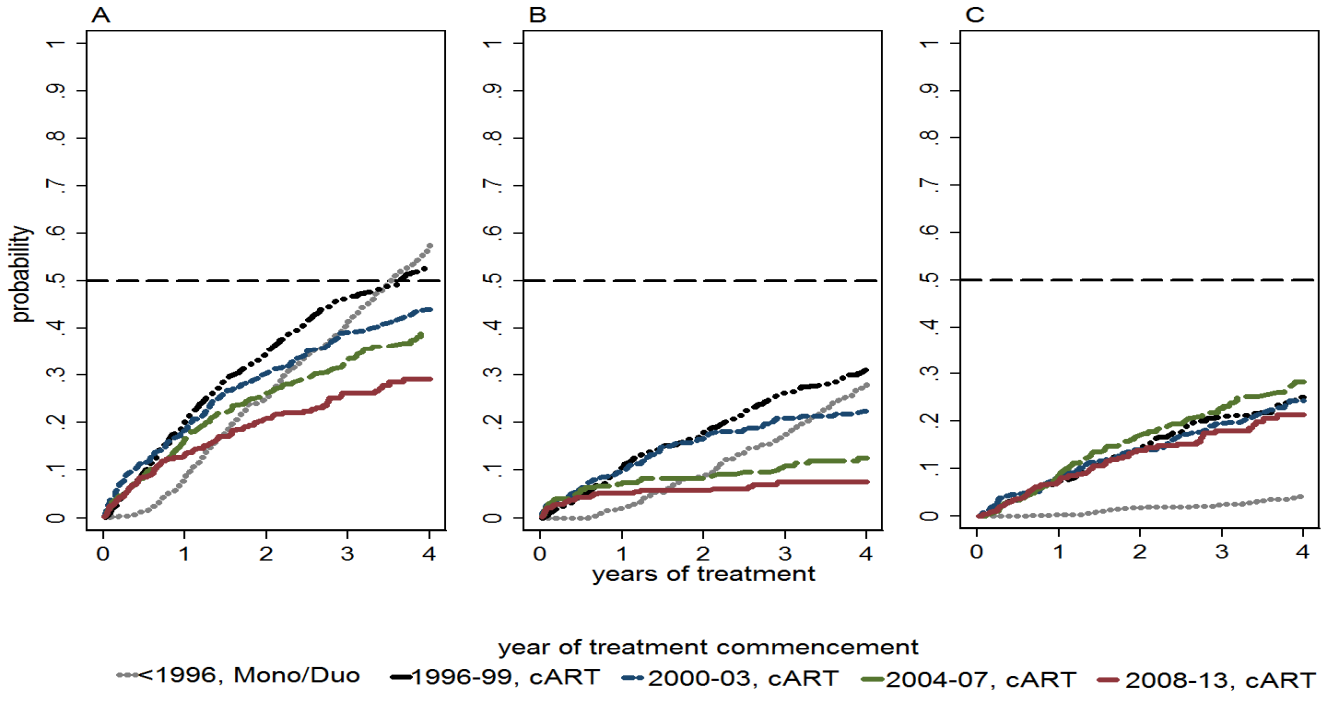


Figure 2: Kaplan-Meier probabilities of time to first switch by era[1]. [A] All switches. [B] Switches with recent virological failure. [C] Switches without recent virological failure.



1. **Kaplan–Meier probabilities of time to first switch with unknown recent virological status not shown**

Table 1: All AHOD demographics[1] (Total – 3 972)

	Number	(%)		Number	(%)
Sex			**CD4 (cells/µl)** [1]		
Male	3654	(92)	<200	426	(11)
Female	309	(8)	200-299	415	(11)
Transgender	9	(0)	300-499	1175	(32)
			500+	1693	(46)
Age (years) [1]			Missing	263	
<30	413	(10)	Mean [SD]	504	[281]
30-39	1421	(36)			
40-49	1290	(32)	**HIV viral load (copies/ml)** [1]		
50+	848	(21)	≤400	2214	(60)
Mean [SD]	42	[10]	401-10 000	616	(17)
			>10 000	831	(23)
Aboriginal/Torres Strait islander[2]			Missing	311	
Yes	42	(1)	Median [LQ – UQ][4]	400	[400-7450]
No	2439	(61)			
Not reported	1491	(38)	**Prior AIDS defining illness**[1]		
			Yes	655	(16)
Exposure category			No	3317	(84)
Male homosexual contact	2896	(73)			
Male homosexual contact and IDU	136	(3)	**Hepatitis C ever**		
Injecting drug user (IDU)	95	(2)	Yes	414	(12)
Heterosexual contact	685	(17)	No	3121	(88)
Receipt of blood/blood products	24	(1)	No test reported	437	
Other	79	(2)			
Missing	57	(1)	**Hepatitis B ever**		
			Yes	170	(5)
Estimated year of HIV infection[3]			No	3139	(95)
<1990	114	(3)	No test reported	663	
1990-1999	610	(15)			
2000-2013	437	(11)	**Total patients under active follow up in last 12 months (N=2244)**[5]		
Missing	2811	(71)			
Patient care Setting			**Recent CD4 (cells/µl)** [6]		
General Practitioner	1391	(35)	< 200	81	(4)
Hospital Tertiary Centre	851	(21)	200-299	107	(5)
Sexual Health Clinic	1730	(44)	300-499	479	(23)
			500+	1374	(67)
Region of birth			Missing	203	
Australia and New Zealand	2131	(54)	Mean [SD]	641	[295]
Asia and Oceania	258	(6)			
Britain and Ireland	142	(4)	**Recent HIV viral load**		
Europe	102	(3)	≤400	1822	94
Africa and Middle East	101	(3)	401-10 000	54	3
North America	40	(1)	>10 000	66	3
South America	41	(1)	Missing	302	
Not reported	1157	(29)	Median [LQ – UQ][4]	400	[400-400]

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 31 sites.
3. Year of HIV infection = mid date between date of first positive and last negative test (coded as not reported 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, 2013 and March 31, 2014.
6. Most recent CD4 count & HIV viral load between March 31, 2013 and March 31, 2014.

Table 2: Follow up status by calendar year

Year	Entered study	Deaths	Lost to Follow up
1999[1]	816	6	37
2000	860	24	45
2001	247	29	66
2002	163	23	62
2003	194	22	61
2004	84	19	78
2005	98	26	65
2006	122	28	63
2007	98	26	86
2008	88	22	85
2009	309	17	78
2010	238	25	87
2011	205	20	96
2012	274	16	158
2013	127	12	91
2014[2]	49	4	0
Total	**3972**	**319**	**1158**

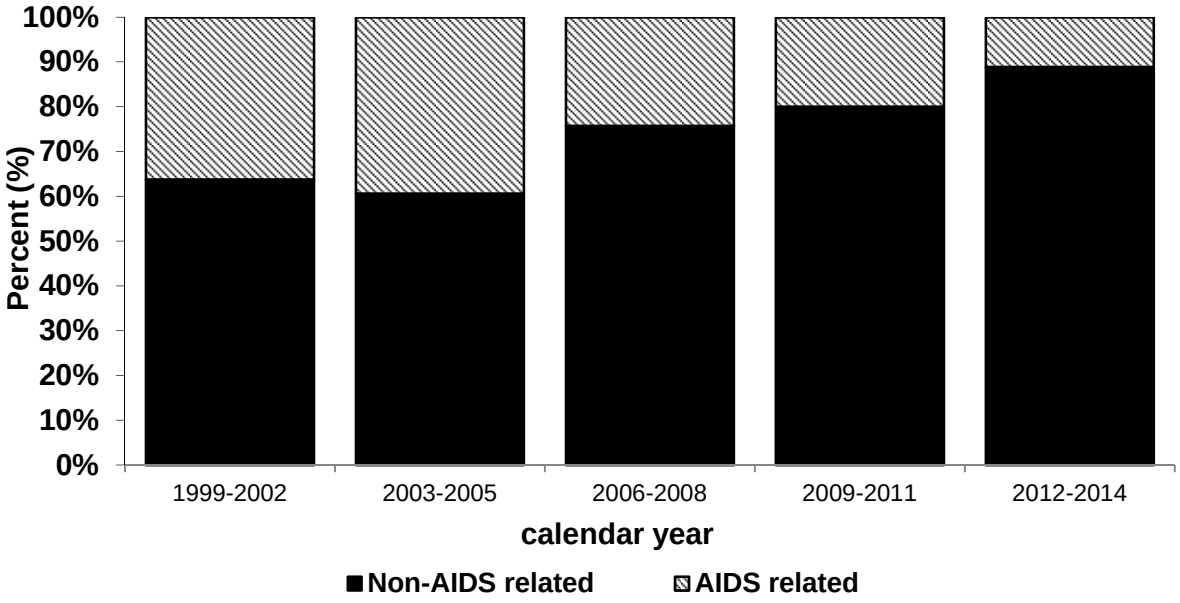
Complete follow-up (percentage of patients)[3]: 71 %

Loss to follow-up (per 100 person years): 4.04 (95% CI: 3.81-4.30)

Mortality (per 100 person years): 1.18 (95% CI: 1.05-1.32)

1. July 1 - December 31, 1999.
2. January 1 - March 31, 2014.
3. Patients who have died or any patients seen at clinic site within the last 12 months (March31, 2013 - March 31, 2014) are considered to have complete follow-up.

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



[1]2012-2014 group includes all deaths reported from 1 January 2014 – 31 March 2014.

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

	1999-2002	2003-2005	2006-2008	2009-2011	2012-2014[1]	All years
Non-AIDS related	51	40	53	36	16	**196**
AIDS related	29	26	17	9	2	**83**
Unknown	2	1	5	6	5	**19**
Missing Coding of Death	0	0	1	11	10	**22**
Total deaths	**82**	**67**	**76**	**62**	**33**	**320**

1. 1 January 2013 to 31 March 2014.

Table 4: Summary of deaths reported in the last 5 year period[1]

Coding of Death Classification[2]	Number
Cancer	17
AIDS (ongoing active disease)	10
Chronic viral hepatitis (progression of / complication to)	5
MI or other ischemic heart disease	3
Suicide	4
Renal failure	3
Other Causes	17
Unknown (autopsy inconclusive, died overseas, etc)	11

1. 1 January 2009 to 31 December 2013.
2. Coding of Death classification (CoDE) – [http://www.cphiv.dk/code/tabid/55/default.aspx].

Table 5: Trends in antiretroviral treatment[1]

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Patients under active follow up[1]	**(n=1988)**	**(n=1989)**	**(n=1990)**	**(n=2021)**	**(n=2028)**	**(n=2005)**	**(n=2109)**	**(n=2250)**	**(n=2199)**	**(n=2357)**	**(n=2299)**
Treatment	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)	**N** (%)
Never treatment	100 (5)	91 (5)	80 (4)	81 (4)	86 (4)	86 (4)	80 (4)	97 (4)	91 (4)	104 (4)	96 (4)
Ever treatment	**n=1888**	**n=1898**	**n=1910**	**n=1940**	**n=1942**	**n=1919**	**n=2029**	**n=2153**	**n=2108**	**n=2253**	**n=2203**
Currently[2]	1571 (79)	1620 (81)	1634 (82)	1713 (85)	1718 (85)	1747 (87)	1880 (89)	2033 (90)	1992 (91)	2197 (93)	2176 (95)
Previously, not currently	317 (16)	278 (14)	276 (14)	227 (11)	224 (11)	172 (9)	149 (7)	120 (5)	116 (5)	56 (2)	27 (1)
Number of drugs ever[3]											
≤3	711 (38)	622 (33)	560 (29)	495 (26)	458 (24)	421 (22)	515 (25)	587 (27)	614 (29)	669 (30)	631 (29)
4-6	786 (42)	798 (42)	779 (41)	760 (39)	767 (39)	743 (39)	748 (37)	788 (37)	770 (36)	857 (38)	881 (40)
7-9	294 (16)	352 (19)	416 (22)	491 (25)	502 (26)	507 (26)	488 (24)	482 (22)	450 (21)	448 (20)	423 (19)
10+	97 (5)	126 (7)	155 (8)	194 (10)	215 (11)	248 (13)	278 (14)	297 (14)	276 (13)	281 (12)	270 (12)
Number of drug classes ever[3,4]											
1	98 (6)	82 (5)	69 (4)	61 (3)	52 (3)	48 (3)	45 (2)	57 (3)	53 (3)	44 (2)	27 (1)
2	1019 (59)	962 (55)	935 (53)	967 (53)	952 (53)	931 (51)	1027 (53)	1087 (53)	1088 (54)	1242 (56)	1235 (56)
3	574 (34)	672 (38)	715 (41)	726 (40)	719 (40)	698 (39)	664 (34)	670 (32)	616 (30)	649 (29)	632 (29)
4	22 (1)	31 (2)	45 (3)	53 (3)	64 (4)	102 (6)	146 (8)	202 (10)	215 (11)	237 (11)	248 (11)
5				3 (0)	15 (1)	30 (2)	47 (2)	54 (3)	58 (3)	57 (3)	59 (3)

1. Treatment status for all patients under active follow during the calendar year. Table includes prospective data only (i.e. records prior to AHOD enrolment are excluded).
2. Currently on treatment is defined as receiving treatment at some point during the calendar year.
3. Denominator is the number of patients who have ever received treatment.
4. Broad class ARV groupings are: nucleos(t)ide reverse transcriptase inhibitors; non-nucleoside reverse transcriptase inhibitors; protease inhibitors; intergrase inhibitors; entry inhibitors;

Table 6: Trends in combination antiretroviral treatment[1]

	2003		2004		2005		2006		2007		2008		2009		2010		2011		2012		2013	
Combination[2]	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
1st combination	328	(19)	322	(18)	305	(17)	268	(15)	241	(13)	234	(13)	352	(18)	361	(17)	392	(19)	490	(22)	451	(21)
2nd combination	369	(21)	350	(20)	311	(18)	319	(18)	344	(19)	340	(19)	335	(17)	408	(20)	407	(20)	482	(22)	506	(23)
3rd combination	316	(18)	318	(18)	308	(17)	297	(16)	283	(16)	277	(15)	259	(13)	293	(14)	280	(14)	305	(14)	325	(15)
≥4th combination	706	(41)	765	(44)	848	(48)	927	(51)	947	(52)	958	(53)	988	(51)	1011	(49)	946	(47)	943	(42)	909	(41)

1. Includes patients who commenced their first combination ART after January 1, 1996 for at least 14 days. The denominator includes all AHOD patients that received combination antiretroviral treatment in any calendar year (i.e. HIV positive), who commenced their first combination ART after January 1, 1996 for at least 14 days. Includes prospective and retrospective data.
2. 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.

Figure 2: Trends in combination antiretroviral treatment (as above)

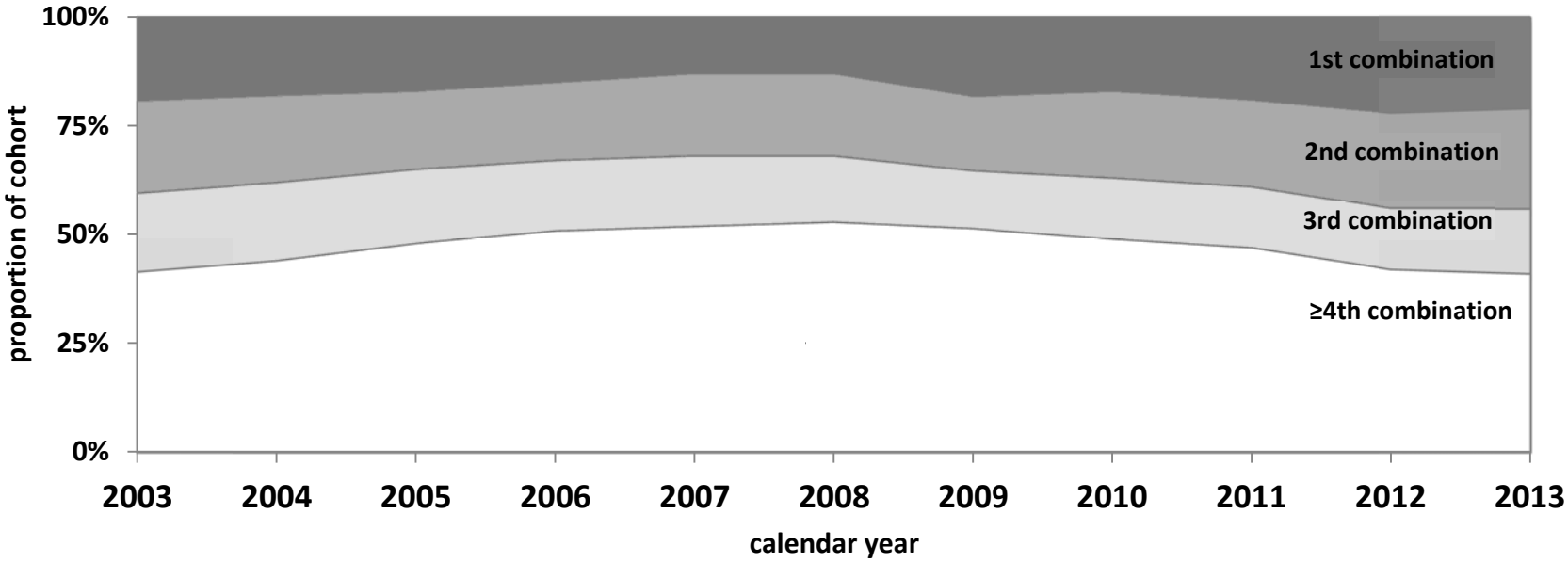


Table 7: Immunological and virological trends[1]

	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Viral load (copies/ml)											
Total N (with measure)	2144	2161	2211	2230	2283	2335	2255	2191	2171	2178	2054
Off Treatment[2]											
No. with a viral load count[4]	473	441	476	414	406	365	301	248	218	154	114
Median	18800	21900	19128	14483	13439	11400	11180	8505	4990	4626	2216
IQR	3680-64000	4370-69300	4138-64100	3600-48050	3000-40738	2278-37000	2027-34926	506-34025	260-41880	50-31549	40-20506
On Treatment[3]											
No. with a viral load count[4]	1671	1720	1735	1816	1877	1970	1954	1943	1953	2024	1940
Median	100	50	50	50	49	49	49	49	40	33	20
IQR	50-875	50-400	49-399	49-71	44-50	40-50	40-50	40-50	30-49	20-49	19-40
CD4 count (cells/µl)											
Total N (with measure)	2157	2177	2222	2217	2285	2322	2282	2243	2230	2242	2155
Off Treatment[2]											
No. with a CD4 count[5]	479	456	489	418	410	370	309	257	220	161	117
Median	488	486	480	505	500	488	513	490	518	557	600
IQR	360-650	370-651	367-650	379-655	397-640	387-660	397-665	397-652	394-675	463-730	471-810
On Treatment[3]											
No. with a CD4 count[5]	1678	1721	1733	1799	1875	1952	1973	1986	2010	2081	2038
Median	493	486	489	503	522	529	540	552	575	586	614
IQR	320-691	315-684	325-693	340-710	360-718	374-740	380-733	398-735	420-768	430-779	441-797

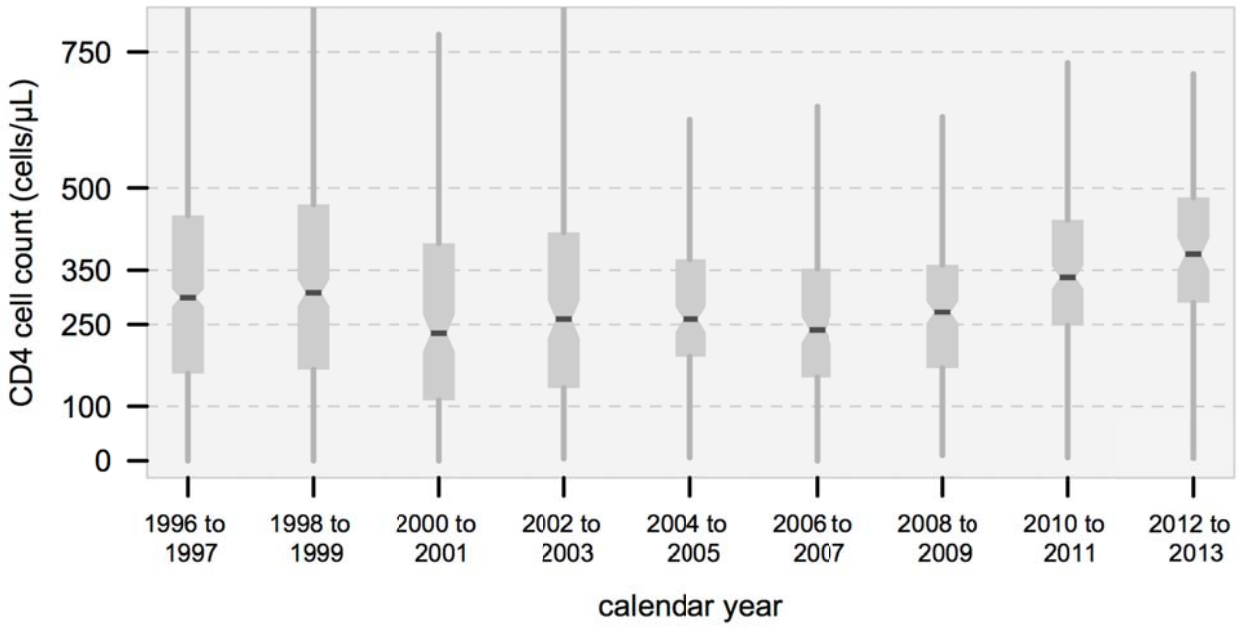
1. Includes retrospective and prospective data. Off treatment if never on a regimen of duration greater than 14 days for given calendar year. Viral load taken as median value during given calendar year. Undetectable assay level taken as ≤50 copies/ml. Data for 2000 and 2001 includes 2 sites with minimum 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.

Table 8: CD4 cell count at antiretroviral therapy initiation by calendar year[1]

	1996 to 1997	1998 to 1999	2000 to 2001	2002 to 2003	2004 to 2005	2006 to 2007	2008 to 2009	2010 to 2011	2012 to 2013
Number of participants initiating ART[1]									
Total N=	780	371	171	159	139	166	206	195	106
CD4 cell count (copies/µl)[2,3]									
Mean	323	346	286	310	325	270	280	347	396
Median	300	309	234	260	260	240	273	337	379
IQR	160-450	165-470	110-400	132-420	190-372	153-353	170-360	247-444	290-484

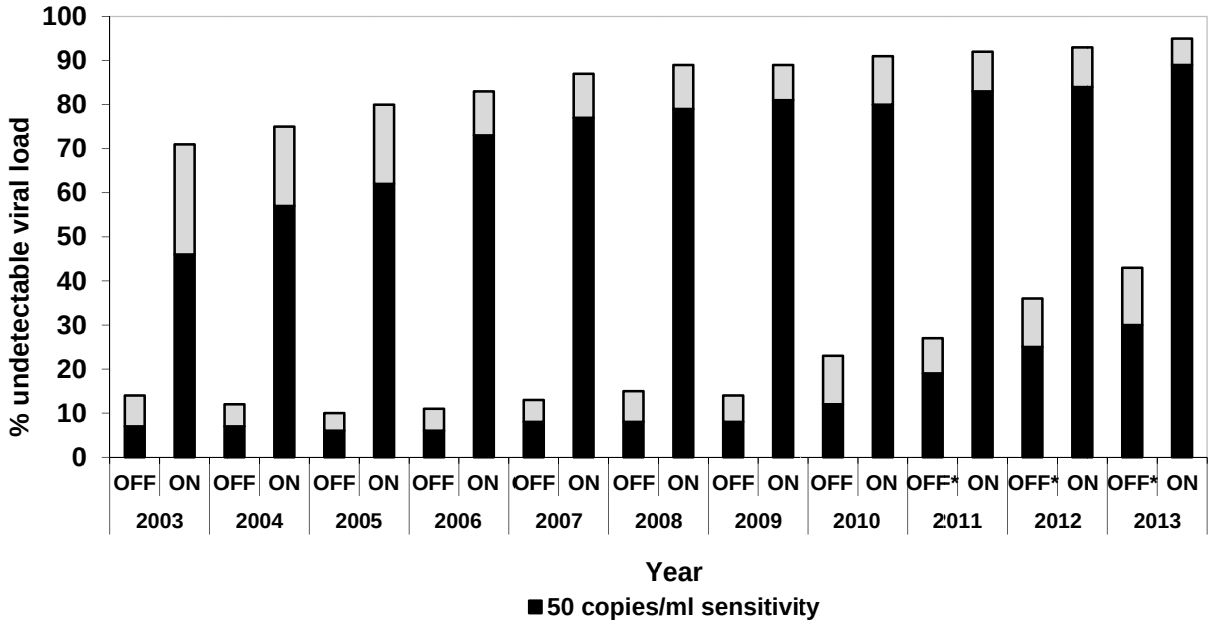
1. First ART defined as a combination of 3 or more antiretroviral agents and a duration of ART>14 days. Includes retrospective and prospective data. ATRAS sub study participants were excluded from analysis.
2. CD4 cell count selected from the observation closest to ART start date within a timeframe window of 12 months prior to ART start date and 1 month post ART start date.
3. A patient was excluded from the analysis if an undetectable viral load was recorded prior to initiating ART or was missing a viral load measurement prior to initiating ART.

Figure 3: Empirical CD4 cell count distribution (boxplot) at antiretroviral therapy initiation by year of ART initation[1-3] (median CD4 indicated by horizontal grey bar)



1. First ART defined as a combination of 3 or more antiretroviral agents and a duration of ART>14 days. Includes retrospective and prospective data. ATRAS sub study participants excluded from analysis.
2. CD4 cell count selected from the observation closest to ART start date within a timeframe window of 12 months prior to ART start date and 7 days post ART start date.
3. A patient was excluded from the analysis if an undetectable viral load was recorded prior to initiating ART or was missing a viral load measurement prior to initiating ART.

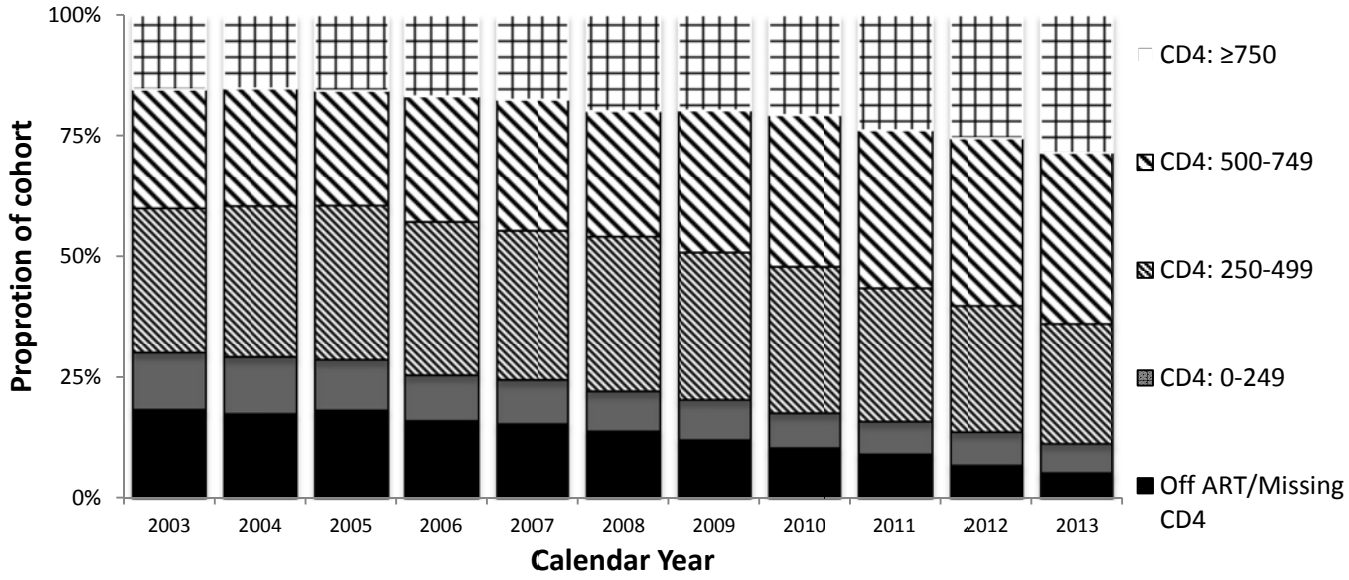
Figure 4: Proportion of patients with an undetectable viral load, by treatment status (off /on treatment) and year according to assay sensitivity[1]



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

* In the "off-treatment" group (n=114), there are 52 patients where their viral load time series is strongly indicative of the patient receiving therapy, defined as 2 or more recent records where pVL <50 copies/ml. Data validation is ongoing with sites.

Figure 5: 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 ART initiation.
3. Patients off treatment include those who have enrolled and have not initiated combination antiretroviral therapy.

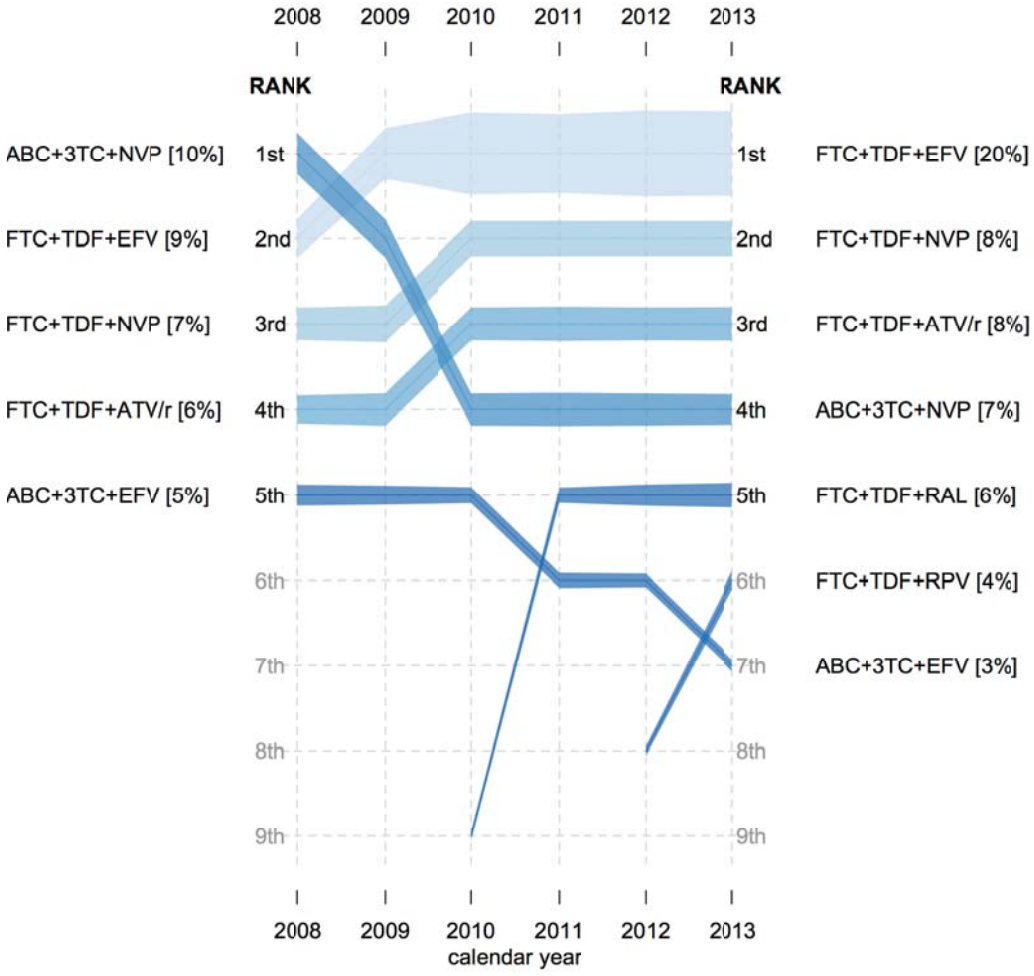
Table 9: Top ten treatment combinations among the AHOD cohort[1]: January-December 2013

In 2013, there were a total of 372 unique antiretroviral treatment (ART) combinations among the 2157 AHOD patients on combination ART. A total of 2474 combination regimens were recorded among these patients throughout 2013. The top ten most common ART combinations are described below.

ART combinations	Number of regimens recorded during 2013
emtricitabine+tenofovir+efavirenz	484
emtricitabine+tenofovir+nevirapine	198
emtricitabine+tenofovir+atazanavir+ritonavir	193
abacavir+lamivudine+nevirapine	172
emtricitabine+tenofovir+raltegravir	141
emtricitabine+tenofovir+rilpivirine	105
abacavir+lamivudine+efavirenz	68
abacavir+lamivudine+atazanavir+ritonavir	56
lamivudine+zidovudine+nevirapine	41
emtricitabine+tenofovir+darunavir+ritonavir	40

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

Figure 6: Top five treatment combinations among the AHOD cohort[1] ranked by proportion[2] of total ART regimens recorded in years 2009-2013



1. Includes retrospective and prospective data. Combinations include 3 or more antiretroviral drugs. Fixed dose combinations are separated into individual component antiretroviral drugs.
2. Proportion defined as frequency of ART line divided by total number of ART regimens recorded. For example, 2013 Rank 1 proportion calculated by 484/2474=19.53%. Thickness of line over time is proportional to calculated percentage.

Table 10: Current use of individual antiretroviral treatments[1]

	2003		2004		2005		2006		2007		2008		2009		2010		2011		2012		2013	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Nucleoside analogue reverse transcriptase inhibitors (NRTI)																						
Abacavir	519	(24)	536	(24)	524	(24)	461	(21)	374	(17)	363	(16)	265	(12)	247	(10)	222	(10)	187	(8)	187	(8)
Combivir[2]	377	(17)	423	(19)	418	(19)	369	(17)	286	(13)	233	(10)	200	(9)	185	(8)	149	(6)	121	(5)	96	(4)
Didanosine	403	(19)	358	(16)	281	(13)	203	(9)	132	(6)	93	(4)	60	(3)	49	(2)	30	(1)	24	(1)	16	(1)
Emtricitabine	-		-		38	(2)	98	(4)	76	(3)	108	(5)	132	(6)	155	(7)	181	(8)	179	(8)	196	(9)
Kivexa[3]	7	(0)	9	(0)	89	(4)	307	(14)	413	(18)	453	(20)	442	(19)	414	(17)	400	(17)	412	(18)	388	(17)
Lamivudine	932	(43)	962	(44)	973	(45)	885	(40)	580	(26)	491	(21)	362	(16)	332	(14)	287	(13)	255	(11)	239	(11)
Stavudine	440	(20)	292	(13)	194	(9)	132	(6)	81	(4)	63	(3)	45	(2)	35	(1)	19	(1)	18	(1)	11	(0)
Tenofovir	514	(24)	616	(28)	735	(34)	761	(34)	507	(23)	466	(20)	433	(19)	410	(17)	383	(17)	347	(15)	329	(15)
Trizivir[4]	170	(8)	158	(7)	151	(7)	124	(6)	87	(4)	70	(3)	56	(2)	45	(2)	36	(2)	26	(1)	17	(1)
Truvada[5]	8	(0)	10	(0)	17	(1)	363	(16)	535	(24)	701	(31)	893	(39)	926	(39)	723	(32)	784	(33)	764	(34)
Zalcitabine	13	(1)	7	(0)	6	(0)	4	(0)	2	(0)	2	(0)	-		-		-		-		-	
Zidovudine	248	(12)	238	(11)	201	(9)	161	(7)	120	(5)	96	(4)	57	(2)	44	(2)	30	(1)	27	(1)	23	(1)
Non-nucleoside analogue reverse transcriptase inhibitors (NNRTI)																						
Delavirdine	18	(1)	17	(1)	12	(1)	11	(0)	9	(0)	3	(0)	2	(0)	2	(0)	-		-		-	
Efavirenz	425	(20)	467	(21)	456	(21)	484	(22)	521	(23)	530	(23)	537	(23)	488	(21)	287	(13)	294	(12)	248	(11)
Nevirapine	670	(31)	667	(30)	640	(29)	621	(28)	638	(28)	658	(29)	643	(28)	613	(26)	546	(24)	537	(23)	482	(21)
Etravirine	-		-		-		2	(0)	24	(1)	52	(2)	82	(4)	101	(4)	107	(5)	112	(5)	111	(5)
Rilpivirine	-		-		-		-		-				2	(0)	2	(0)	3	(0)	13	(1)	25	(1)

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.

Table 10 continued: Current use of individual antiretroviral treatments[1]

	2003		2004		2005		2006		2007		2008		2009		2010		2011		2012		2013	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Protease Inhibitor (PI)																						
Amprenavir	69	(3)	52	(2)	45	(2)	30	(1)	28	(1)	27	(1)	27	(1)	24	(1)	19	(1)	17	(1)	15	(1)
Atazanavir	135	(6)	265	(12)	390	(18)	442	(20)	477	(21)	530	(23)	541	(24)	547	(23)	513	(22)	496	(21)	450	(20)
Darunavir	-		8	(0)	14	(1)	41	(2)	73	(3)	117	(5)	161	(7)	194	(8)	221	(10)	247	(10)	248	(11)
Fosamprenavir	-		2	(0)	31	(1)	36	(2)	32	(1)	30	(1)	24	(1)	17	(1)	15	(1)	13	(1)	11	(0)
Indinavir	181	(8)	123	(6)	69	(3)	44	(2)	30	(1)	20	(1)	10	(0)	6	(0)	4	(0)	4	(0)	4	(0)
Kaletra[6]	405	(19)	425	(19)	423	(19)	392	(18)	370	(16)	344	(15)	318	(14)	310	(13)	254	(11)	219	(9)	179	(8)
Nelfinavir	136	(6)	104	(5)	71	(3)	47	(2)	35	(2)	9	(0)	8	(0)	7	(0)	6	(0)	6	(0)	5	(0)
Ritonavir	358	(17)	438	(20)	533	(24)	608	(27)	626	(28)	678	(30)	683	(30)	713	(30)	701	(31)	721	(31)	666	(30)
Saquinavir	159	(7)	138	(6)	126	(6)	109	(5)	89	(4)	70	(3)	44	(2)	35	(1)	32	(1)	28	(1)	24	(1)
Entry Inhibitor (EI)																						
Enfurvitide	44	(2)	54	(2)	61	(3)	67	(3)	60	(3)	44	(2)	28	(1)	18	(1)	10	(0)	7	(0)	6	(0)
Maraviroc	-		-		9	(0)	7	(0)	8	(0)	15	(1)	22	(1)	29	(1)	32	(1)	41	(2)	46	(2)
Integrase Inhibitors (II)																						
Raltegravir	-		-		-		8	(0)	62	(3)	173	(8)	294	(13)	423	(18)	460	(20)	527	(22)	533	(24)
Elvitegravir	-		-		-		-		-		-		-		-		-		7	(0)	8	(0)
Dolutegravir	-		-		-		-		-		-		-		-		-		4	(0)	17	(1)
Class Combinations (FDC)																						
Atripla[7]	-		-		-		-		2	(0)	3	(0)	12	(1)	264	(11)	346	(15)	378	(16)	370	(16)
Eviplera[8]	-		-		-		-		-		-		-		-		3	(0)	50	(2)	93	(4)
Stribild[9]	-		-		-		-		-		-		-		-		-		-		2	(0)

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. **6**. Kaletra – lopinavir & ritonavir.
7. Atripla – tenofovir & emtricitabine & efavirenz. **8**. Eviplera - tenofovir & emtricitabine & rilipivirine. **9**. Stribild - tenofovir & emtricitabine & elvitegravir & cobicistat.

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 patient's 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 caution our estimates for 2011- 2013 data for Table 11. We are working with the producers of the HSD Report to amend these issues and are currently revisiting our methodology for these figures.

Table 11: 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	**2009**	**2010**	**2011**	**2012**	**2013**
Nucleoside analogue reverse transcriptase inhibitors	544	492	473	425	400
Abacavir	229	163	117	84	60
Didanosine	131	211	146	157	60
Emtricitabine	921	822	718	609	540
Lamivudine	104	77	48	36	20
Stavudine	156	128	98	70	60
Zidovudine	846	719	602	461	400
Lamivudine & Zidovudine	2243	2220	2179	2041	2500
Abacavir & Lamivudine	240	163	133	103	100
Abacavir, Lamivudine & Zidovudine	1294	1586	1967	2039	2480
Tenofovir	5246	4772	4510	4404	4340
Tenofovir & Emtricitabine	544	492	473	425	400
Non-nucleoside analogue reverse transcriptase inhibitors					
Delavirdine	7	6	-	-	-
Efavirenz	2996	2003	973	738	700
Nevirapine	2791	2809	2728	2376	2260
Etravirine	155	403	456	454	520
Rilpivirine	-	-	-	18	40
Protease inhibitors					
Atazanavir	2609	2879	2906	2582	2380
Darunavir	685	887	1058	1131	1140
Fosamprenavir	219	181	148	111	80
Indinavir	52	31	21	18	20
Lopinavir & ritonavir	1871	1734	1581	1341	960
Ritonavir	2850	3181	3098	2652	3180
Saquinavir	148	121	95	72	40
Tipranavir	27	20	15	11	<5
Entry inhibitors					
Enfuvirtide	60	37	22	13	20
Maraviroc	-	55	118	122	160
Integrase inhibitor					
Raltegravir	821	1250	1848	2250	2740
Combination Class Agents					
Tenofovir, Emtricitabine & Efavirenz	-	2013	2873	2786	3100
Tenofovir, Emtricitabine & Rilpivirine	-	-	-	217	1040
Total patients[3]	**10,900**	**12,400**	**12,700**	**12,800**	**13,700**
Total cost[4] ($'000s)	**156,810**	**181,508**	**200,165**	**210,005**	**229,000**

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 to December 2012 estimated from the HSD Program Public Hospital Dispensed National Pack Number Report because of changes to S100 data collection methodology. Number of person years for January 2013 onwards estimated from the PBS item reports on services and benefits.
2 Dashes (-) indicate that data were not available.
3 Total patients calculated as (Lamivudine + Combivir (Lamivudine & Zidovudine)+Trizivir (Abacavir, Lamivudine & Zidovudine)+Kivexa (Abacavir & Lamivudine)+Emtricitabine +Truvada(Tenofovir & Emtricitabine) + Atripla(Tenofovir & Emtricitabine & Efavirenz) + Exiplera(Tenofovir & Emtricitabine & Rilpivirine))/the proportion of patients in the Australian HIV Observational Database receiving any of the previously mentioned drugs in each year. Estimates of total patients are rounded to nearest 100 patients.
4 Public Hospital Expenditure.

Source: Highly Specialised Drugs (S100) Program

Notes:

Notes:

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