

Supplementary Material

Lifetime cost of HIV management in Australia: an economic model

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Supplementary Tables

Table S1 summarises the proportion of people living with HIV in Australia according to their CD4 count and current line of ART.

Table S1: Initial proportion of the cohort in each health state

CD4 Category	Line of ART	Base case	Source
<50	No ART	0.0017	17
	1st line	0.0243	J. Hutchinson, personal communication, July 31, 2020
	2nd line	0.0018	
	3rd line	0.0009	
50-200	No ART	0.0015	17
	1st line	0.0212	J. Hutchinson, personal communication, July 31, 2020
	2nd line	0.0016	
	3rd line	0.0008	
201-350	No ART	0.0037	17
	1st line	0.0521	J. Hutchinson, personal communication, July 31, 2020
	2nd line	0.0048	
	3rd line	0.0010	
351-500	No ART	0.0085	17
	1st line	0.1198	J. Hutchinson, personal communication, July 31, 2020
	2nd line	0.0110	
	3rd line	0.0023	
>500	No ART	0.1338	17
	1st line	0.5886	J. Hutchinson, personal communication, July 31, 2020
	2nd line	0.0202	
	3rd line	0.0006	

Table S2 summarises the transition and event probability parameters according to their CD4 count and current line of ART. All probability parameters are applied on a 6-monthly basis in the Markov model

Table S2: Transition and event probability parameters.

	CD4 Category		Base case	Lower limit	Upper limit	Reference range	Source
Probability of an HIV-related hospitalisation	<100		0.0014	0.0012	0.0016	95% CI	15
	100-200		0.0008	0.0007	0.0010		
	201-350		0.0013	0.0012	0.0014		
	351-500		0.0007	0.0006	0.0008		
	>500		0.0007	0.0006	0.0009		
CD4 progression when not on ART	From 50-200	to <50	0.2847	0.1975	0.3560	95% CI	18
	From 201-350	to 50-200	0.1263	0.1175	0.1350		
	From 351-500	to 201-350	0.1521	0.1479	0.1521		
	From >500	to 351-500	0.4084	0.3495	0.5529		
CD4 progression when on ART	From <50	to 50-200	0.0540	0.0232	0.2453	95% CI	18
	From 50-200	to 200-350	0.0568	0.0159	0.2904		
	From 50-200	to <50	0.0440	0.0095	0.3034		
	From 200-350	to 50-200	0.0778	0.0247	0.3524		
	From 350-500	to 200-350	0.0488	0.0109	0.3527		
	From >500	to 350-500	0.0129	0.0025	0.1285		
Probability of ART line switches	<200	No ART to 1 st line	0.0932	0.0577	0.4204	95% CI	J. Hutchinson, personal communication, July 31, 2020
		1 st line to 2 nd line	0.1317	0.1070	0.2387		
		2 nd line to 3 rd line	0.1337	0.0638	0.4202		
	200-500	No ART to 1 st line	0.1009	0.0659	0.6988		
		1 st line to 2 nd line	0.0896	0.0682	0.1618		
		2 nd line to 3 rd line	0.2387	0.1662	0.6312		
	>500	No ART to 1 st line	0.1018	0.0666	0.4204		
		1 st line to 2 nd line	0.1034	0.0750	0.1993		
		2 nd line to 3 rd line	0.1416	0.0991	0.1841		
Proportion initiating ART	<50		0.9	0.63	0.99	95% CI	17
	50-200		0.6838	0.4786	0.8889		
	200-350		0.5528	0.3870	0.7186		
	350-500		0.2929	0.2050	0.3808		

	>500	0.1056	0.0739	0.1372		
All-cause mortality when on ART	<50	0.1061			95% CI	¹⁶
	51-200	0.0169				
	201-350	0.0040				
	351-500	0.0020				
	>500	0.0010				
All-cause mortality for those not on ART	<50	0.1491			95% CI	¹⁸
	50-200	0.0291				

Table S3 uses data from the Australian Bureau of Statistics and is converted to 6-monthly probabilities using the formula $p=1-e^{-rate*time}$.^{14,29} We weighted these according to the male: female ratio in the AHOD cohort.³⁰ These figures are used as the background age-specific mortality in the model.

Table S3: 6-month all-cause probability of death, weighted 89.3% male and 10.7% female

Age	6-month probability	Age	6-month probability	Age	6-month probability
30	0.000361	58	0.002687	86	0.045361
31	0.00377	59	0.002933	87	0.051026
32	0.00396	60	0.003196	88	0.057244
33	0.000420	61	0.003472	89	0.064022
34	0.000450	62	0.003760	90	0.071159
35	0.000479	63	0.004056	91	0.078695
36	0.000512	64	0.004386	92	0.086575
37	0.000545	65	0.004754	93	0.094606
38	0.000579	66	0.005172	94	0.102445
39	0.000618	67	0.005638	95	0.107184
40	0.000652	68	0.006175	96	0.111720
41	0.000701	69	0.006791	97	0.117712
42	0.000750	70	0.007500	98	0.126669
43	0.000809	71	0.008296	99	0.140466
44	0.000882	72	0.009185	100	0.155747
45	0.000957	73	0.010186		
46	0.001037	74	0.011268		
47	0.001113	75	0.012483		
48	0.001192	76	0.013906		
49	0.001275	77	0.015568		
50	0.001368	78	0.017479		
51	0.001484	79	0.019624		
52	0.001613	80	0.022087		
53	0.001765	81	0.024873		
54	0.001931	82	0.027998		
55	0.002098	83	0.031504		
56	0.002277	84	0.035590		
57	0.002467	85	0.040228		

Table S4 describes the six-monthly costs accrued in accordance to the line of antiretroviral (ART), CD4 counts, and transition between health states. Details of the cost derivations are described in Tables S5–S9.

Table S4: Six-monthly costs of ART drugs, prophylaxis, medical services and lab tests (2019

Australian dollars)

Cost Category	Cost Item	Cost (2019 AUD)	Source
ART	1st line	\$5,585.25	20
	2nd line	\$8,219.18	20
	3rd line	\$12,202.50	20
Prophylaxis for opportunistic infections	CD4 50-200	\$253.34	20
	CD4 <50	\$1,474.08	20
Medical services	Hospitalisation	\$19,348.80	31
	Routine consultations	\$111.34	23
Lab tests	Initial testing	\$1966.15	23
	ART switch	\$1694.03	23
	Routine check-up	\$476.85	23

Table S5 describes the individual drugs (ART and prophylaxis) used in each line of HIV treatment and their corresponding six-monthly costs. Patented drug costs were taken from the Pharmaceutical Benefits Scheme²⁰, while currently available generic drug prices were taken from the Inhouse Pharmacy website^{20,32}.

Table S5: Six-monthly costs of drugs (2019 Australian dollars)

Drug names		Patented drugs ²⁰	Generic drugs ³²
1st line ART	Dolutegravir/ Lamivudine/ Abacavir	\$5,183.88	N.A.
	Bictegravir/ Emtricitabine/ Tenofovir alafenamide	\$5,610.72	\$1,566.28
	Elvitegravir/Emtricitabine/Cobicistat/Tenofovir alafenamide	\$5,961.13	N.A.
2nd line ART	Emtricitabine/ tenofovir alafenamide	\$3,824.32	\$689.16
	+ Darunavir/ Cobicistat	\$4,394.86	N.A.
3rd line ART	Dolutegravir	\$3,983.32	\$1,215.44
	+ Emtricitabine/ Tenofovir alafenamide	\$3,824.32	\$689.16
	+ Darunavir/ Cobicistat	\$4,394.86	N.A.
Prophylaxis for opportunistic infections	CD4 <200: Cotrimoxazole	\$253.34	N.A.
	CD4 <50: Valaciclovir / Famaciclovir	\$159.54	N.A.
	CD4 <50: + Azithromycin	\$720.43	N.A.
	CD4 <50: + Fluconazole	\$340.77	N.A.

Table S6 describes the mean hospitalisation costs associated with the six-monthly probability of hospitalisation, summarised below. Costs were taken from the Australian Refined Diagnosis Related Groups were categorised as “major complexity”, “intermediate complexity”, and “minor complexity”. We assumed that there is an equal probability of each complexity among those hospitalised.

Table S6: Hospitalisation costs by complexity category and probabilities of hospitalisation (2019 Australian Dollars)

HIV-related DRG code	Cost	Source
Major complexity	\$42,486.60	³¹
Intermediate complexity	\$12,059.74	²⁰
Minor complexity	\$3,500.08	²⁰
Average	\$19,348.80	

Table S7 describes the medical and laboratory costs associated with a PLHIV starting first-line ART.

Consultation and laboratory unit costs were taken from the Medical Benefits Schedule.²³

Table S7: Cost of initial testing after HIV diagnosis.

Routine medical consultations	No. per 6-months	% of patients receiving the item	Unit cost²³	Weighted costs (2019 AUD)
GP consultations	2	56%	38.20	42.78
Specialist consultations	2	44%	77.90	68.55
Total medical				111.34
Routine laboratory tests				
HIV viral load	2	100%	180.25	360.50
Full blood count	2	100%	16.95	33.90
CD4 count	2	100%	197.35	394.70
Genotype testing for HIV	1	100%	770.30	770.30
Glucose	1	100%	9.70	9.70
Lipids	1	100%	9.70	9.70
Liver function test	2	100%	17.70	35.40
Urea and electrolytes	2	100%	17.70	35.40
Syphilis serology	1	100%	29	29
Hep A Ab	1	100%	40.55	40.55
Hep B Ab, sAg, cAb	1	100%	40.55	40.55
Hep C Ab or PCR	1	100%	40.55	40.55
HLA B5701	1	100%	40.55	40.55
Calcium	1	100%	9.70	9.70
Phosphate	1	100%	9.70	9.70
Vitamin D	1	100%	30.05	30.05
QuantiFERON-TB Gold	1	100%	34.90	34.90
Urine biochemistry	1	100%	9.70	9.70
Toxoplasmosis serology	1	100%	15.65	15.65
CMV serology	1	100%	15.65	15.65
Total laboratory cost				1966.15

Table S8 describes the medical and laboratory costs associated with a PLHIV who has experienced viral load failure, requiring a change in the line of ART. Consultation and laboratory unit costs were taken from the Medical Benefits Schedule.²³

Table S8: Cost of switching antiretroviral therapy after the patient experienced viral load failure.

Routine medical consultations	No. per 6-months	% of patients receiving the item	Unit cost ²³	Weighted costs (2019 AUD)
GP consultations	1	56%	38.20	21.39
Specialist consultations	1	44%	77.90	34.28
Total medical				111.34
Routine laboratory tests				
HIV viral load	2	100%	180.25	360.50
Full blood count	2	100%	16.95	33.90
CD4 count	2	100%	197.35	394.70
Genotype testing for HIV	1	100%	770.30	770.30
Glucose	0.5	100%	9.70	4.85
Lipids	0.5	100%	9.70	4.85
Liver function test	2	100%	17.70	35.40
Urea and electrolytes	2	100%	17.70	35.40
Syphilis serology	1	100%	29	29
Urine biochemistry	0.5	100%	9.70	4.85
Hep C Ab or PCR	0.5	100%	40.55	20.28
Total laboratory cost				1694.03

Table S9 describes the medical and laboratory costs for a PLHIV with a controlled viral load during routine six-monthly check-ups. Consultation and laboratory unit costs were taken from the Medical Benefits Schedule.²³

Table S9: Cost of routine medical consultations and laboratory tests as part of routine check-ups.

Routine medical consultations	No. per 6-months	% of patients receiving the item	unit cost²³	Weighted costs (2019 AUD)
GP consultations	2	56%	38.20	42.78
Specialist consultations	2	44%	77.90	68.55
Total medical				111.34
Routine laboratory tests				
HIV viral load	1	100%	180.25	180.25
Full blood count	1	100%	16.95	16.95
CD4 count	1	100%	197.35	197.35
Glucose	0.5	100%	9.70	4.85
Lipid	0.5	100%	9.70	4.85
Liver function test	1	100%	17.7	17.70
Urea and electrolytes	1	100%	17.7	17.70
Syphilis serology	0.5	100%	29	14.5
Urine biochemistry	0.5	50%	9.70	2.43
Hep C Ab or PCR	0.5	100%	40.55	20.28
Total laboratory cost				476.85

Table S10 describes the range of parameter inputs used in the tornado diagrams (upper- and lower-limits) and the source of the range of parameter inputs used for the probabilities and cost items in the model.

Table S10: Parameter base case values and ranges used in the tornado diagrams.

Probabilities	6-month probability			Reference range
	Base case	Lower limit	Upper limit	
CD4 decline (no ART) from CD4 50-200 to <50	0.2847	0.1975	0.3560	95% CI
CD4 decline (no ART) from CD4 201-350 to 50-200	0.1263	0.1175	0.1350	95% CI
CD4 decline (no ART) from CD4 351-500 to 201-350	0.1521	0.1479	0.1521	95% CI
CD4 decline (no ART) from CD4 >500 to 351-500	0.4084	0.3495	0.5529	95% CI
Starting ART for CD4 <50	0.9	0.63	0.99	95% CI
Starting ART for CD4 50-200	0.6838	0.4786	0.8889	95% CI
Starting ART for CD4 201-350	0.5528	0.3870	0.7186	95% CI
Starting ART for CD4 351-500	0.2929	0.2050	0.3808	95% CI
Starting ART for CD4 >500	0.1056	0.0739	0.1372	95% CI
CD4 decline (with ART) from CD4 50-200 to <50	0.0440	0.0095	0.3034	95% CI
CD4 decline (with ART) from CD4 201-350 to 50-200	0.0778	0.0247	0.3524	95% CI
CD4 decline (with ART) from CD4 351-500 to 201-350	0.0488	0.0109	0.3527	95% CI
CD4 decline (with ART) from CD4 >500 to 351-500	0.0129	0.0025	0.1285	95% CI
CD4 improvement (with ART) from CD4 <50 to 50-200	0.0540	0.0232	0.2453	95% CI
CD4 improvement (with ART) from CD4 50-200 to 201-350	0.0568	0.0159	0.2904	95% CI
1st line to 2nd line ART switch for CD4 <200	0.0932	0.0577	0.4204	95% CI
2nd line to 3rd line ART switch for CD4 <200	0.1317	0.1070	0.2387	95% CI
3rd line ART failure for CD4 <200	0.1337	0.0638	0.4202	95% CI
1st line to 2nd line ART switch for CD4 201-500	0.1009	0.0659	0.6988	95% CI
2nd line to 3rd line ART switch for CD4 201-500	0.0896	0.0682	0.1618	95% CI
3rd line ART failure for CD4 201-500	0.2387	0.1662	0.6312	95% CI
1st line to 2nd line ART switch for CD4 >500	0.1018	0.0666	0.4204	95% CI
2nd line to 3rd line ART switch for CD4 >500	0.1034	0.0750	0.1993	95% CI
3rd line ART failure for CD4 >500	0.1416	0.0991	0.1841	95% CI
Death (on ART) for CD4 <50	+ 0.1050	N.A.	N.A.	±30%
Death (on ART) for CD4 50-200	+ 0.0157	N.A.	N.A.	±30%
Death (on ART) for CD4 201-350	+ 0.0029	N.A.	N.A.	±30%
Death (on ART) for CD4 351-500	+ 0.0009	N.A.	N.A.	±30%
Death (on ART) for CD4 >500	- 0.0001	N.A.	N.A.	±30%
Death (no ART) for CD4 <50	0.1491	0.1376	0.1943	95% CI
Death (no ART) for CD4 50-200	0.0291	0.0266	0.0387	95% CI
Hospitalisation for CD4 <50	0.0014	0.0012	0.0016	95% CI
Hospitalisation for CD4 50-200	0.0008	0.0007	0.0010	95% CI
Hospitalisation for CD4 201-350	0.0013	0.0012	0.0014	95% CI
Hospitalisation for CD4 351-500	0.0007	0.0006	0.0008	95% CI
Hospitalisation for CD4 >500	0.0007	0.0006	0.0009	95% CI
Cost items				
Hospitalisation	19,348.80	13,544.16	25,153.44	±30%
Prophylaxis for CD4 50-200	253.34	177.34	329.34	±30%
Prophylaxis for CD4 <50	1,474.08	1,031.86	1,916.30	±30%
1st line ART	5,585.25	3,909.68	7,260.83	±30%
2nd line ART	8,219.18	5,753.43	10,684.93	±30%
3rd line ART	12,202.50	8,541.75	15,863.25	±30%
GP consultation	38.20	26.74	49.66	±30%
Specialist consultation	77.90	54.53	101.27	±30%
Total consultation (GP consultation * 0.56 + specialist consultation* 0.44)	55.67	38.97	72.37	±30%
Cost of initial testing (total consultation + lab test)	2,077.49	1,454.24	2,700.73	±30%
Cost of switching ART (total consultation + lab test)	1,805.36	1,263.75	2,346.97	±30%
Cost of routine check-ups (total consultation + lab test)	532.52	372.76	692.27	±30%
HIV RNA test	180.25	126.18	234.33	±30%
Full blood count test	16.95	11.87	22.04	±30%
CD4 count test	197.35	138.145	256.56	±30%
Genotype testing	770.30	539.21	1,001.39	±30%
glucose/lipid test	9.70	6.79	12.61	±30%
Liver function & urea/electrolytes test	17.70	12.39	23.01	±30%
Syphilis serology test	29	20.30	37.70	±30%
Hepatitis A, B, C, HLA B	40.55	28.39	52.72	±30%

Calcium & phosphate test	9.70	6.79	12.61	±30%
Vitamin D test	30.05	21.04	39.07	±30%
QuantiFERON-TB Gold test	34.90	24.43	45.37	±30%
Urine biochemical test	9.70	6.79	12.61	±30%
Toxoplasmosis/cytomegalovirus serology	15.65	10.96	20.35	±30%
Lab costs (initial testing)	1,966.15	1,376.31	2,556	±30%
Lab costs (ART switches)	1,694.02	1,185.82	2,202.23	±30%
Lab costs (routine testing)	476.85	333.80	619.91	±30%

Table S11 describes the parameter inputs (mean and standard deviation) and distributions used in the probabilistic sensitivity analysis (PSA). Only the top 11 cost and top 11 probability parameters that had the largest impact on the lifetime cost were converted into distributions for analysis. The standard deviations were calculated using the range of the 95% confidence intervals divided by 1.92 where available. Where it was not provided, it was varied as $0.3 \times \text{mean}$

Table S11 parameters used in the Probabilistic Sensitivity Analysis (PSA)

Probabilities	Mean	S.D.	Distribution
CD4 decline (with ART) from CD4 50-200 to <50	0.0440	0.3 * 0.0440	Beta
CD4 decline (with ART) from CD4 201-350 to 50-200	0.0778	0.3 * 0.0778	Beta
CD4 decline (with ART) from CD4 351-500 to 201-350	0.0488	0.3 * 0.0488	Beta
CD4 decline (with ART) from CD4 >500 to 351-500	0.0129	0.3 * 0.0129	Beta
CD4 improvement (with ART) from CD4 50-200 to 201-350	0.0568	0.3 * 0.0568	Beta
3rd line ART failure for CD4 <200	0.1337	0.3 * 0.1337	Beta
3rd line ART failure for CD4 201-500	0.2387	0.3 * 0.2387	Beta
2nd line to 3rd line ART switch for CD4 >500	0.1034	0.3 * 0.1034	Beta
3rd line ART failure for CD4 >500	0.1416	0.3 * 0.1416	Beta
Death (on ART) for CD4 <50	t_mortality [_stage] + 0.1050	0.3 * (t_mortality [_stage] + 0.1050)	Beta
Cost items			
Prophylaxis for CD4 <50	1,474.08	0.3 * 1,474.08	Gamma
1st line ART	5,585.25	0.3 * 5,585.25	Gamma
2nd line ART	8,219.18	0.3 * 8,219.18	Gamma
3rd line ART	12,202.50	0.3 * 12,202.50	Gamma
Total consultation (GP consultation * 0.56 + specialist consultation* 0.44)	55.67	0.3 * 55.67	Gamma
Cost of switching ART (total consultation + lab test)	1,805.36	0.3 * 1,805.36	Gamma
Cost of routine check-ups (total consultation + lab test)	532.52	0.3 * 532.52	Gamma
HIV RNA test	180.25	0.3 * 180.25	Gamma
CD4 count test	197.35	0.3 * 197.35	Gamma
Lab costs (ART switches)	1,694.02	0.3 * 1,694.02	Gamma
Lab costs (routine testing)	476.85	0.3 * 476.85	Gamma