Assessing the benefits of rapid start antiretroviral therapy for newly diagnosed people with HIV in the United States

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Supplemental Appendix 1 – Economic Model Additional Information

Inputs utilized to populate the economic model included the baseline distribution of ART initiation timepoints, CD4 state transition probabilities, probabilities of viral suppression over time, HIV transmission inputs, and cost inputs. This section provides additional detail on the inputs related to CD4 health state transitions, costs, and onward HIV transmission.

Separate CD4 state transitions were applied to individuals on and off treatment. Off treatment CD4 transitions were sourced from a published natural history study investigating CD4 cell progression among untreated PWH [1]. On treatment transitions were informed by a published appraisal by the UK National Institute of Health and Care Excellence (NICE) [2]. In total, five sets of transitions were modeled:

- Off treatment – No viral suppression
- On treatment – No viral suppression (weeks 0-48)
- On treatment – No viral suppression (week 49+)
- On treatment – Viral suppression (weeks 0-48)
- On treatment – Viral suppression (week 49+)

Full details of these transitions are included in **Supplemental Appendix 2**.

Each CD4 health state was assigned a per-cycle cost, reflecting healthcare use such as non-HIV medication and hospital visits from a published evaluation of lifetime HIV-related medical costs in the US [3]. A weekly ART cost was applied to individuals on treatment using results of a US observational study [4]. These costs are outlined in Table S1, reflecting per cycle costs inflated to 2025 using relevant US indices [5]. A discount rate of 3% was applied to all costs in line with recommendations for economic evaluations in the US context [6, 7].

Table S1: ART and CD4 health state costs (weekly cost)

Cost	Value	Source
CD4: <50	$842.41	Bingham et al. 2021 [3]
CD4: 50-199	$378.09	
CD4: 200-349	$202.61	
CD4: 350-500	$143.51	
CD4: >500	$106.71	
ART cost	$837.18	Cohen 2025 [4]

Abbreviations: *ART, antiretroviral therapy; CD4, cluster of differentiation 4.*

A key element of rapid start ART is ensuring PWH achieve viral suppression as soon as possible, therefore reducing the likelihood of transmission to the susceptible population. New infections were calculated based on a per-act transmission probability by viremic individuals (both for those on treatment and off treatment) accounting for the average number of risk acts per cycle, both taken from published sources [8, 9]. Separate probabilities were generated for three core groups: heterosexual men, heterosexual women, and men who have sex with men (MSM). These were subsequently combined with the distribution of new HIV infections for each group from the latest report by the Centers for Disease Control and Prevention (CDC) to obtain a weighted probability that was applied

to the full cohort [10]. Table S2 summarizes inputs related to transmission among individuals who were not virally suppressed.

Table S2: HIV transmission inputs

Input	On Treatment	Off Treatment	Source
Per-act transmission probability			
Heterosexual men	0.0001	0.00159	Supervie et al. 2017 [8]
Heterosexual women	0.00021	0.00318	
MSM	0.00134	0.01767	
Average risk acts per week	0.6209		Estrada et al. 2022 [9]
Average weekly transmissions	0.00058	0.00778	Calculation/CDC 2024 [10]

Abbreviations: *MSM, men who have sex with men.*

In order to capture the cost savings from averting one onward HIV transmission, the mean excess healthcare costs for a PWH compared to a person without HIV were sourced from a published analysis of observational study data [4]. This study reported mean discounted lifetime excess healthcare costs of $1,117,729 for a PWH, which were inflated to a value of $1,164,171 and applied in the analysis.

Medicaid-covered Population Scenario

A key scenario analysis relates to the specific time points at which individuals can start ART. Given the high degree of variation in commencement patterns across geographic areas and populations in the US, the timepoints at which individuals can start ART was updated to reflect published results among a cohort of Medicaid-covered PWH [11]. Table S3 presents the updated time points and inputs for this scenario.

Table S3: Comparators ART start time distributions – Medicaid covered population

ART Commencement Period	Standard of Care Cohort	Early Start Cohort
2 weeks	20.4%	40.80%
8 weeks	36.4%	27.07%
26 weeks	26.0%	19.34%
52 weeks	17.2%	12.79%

Abbreviations: *ART, antiretroviral therapy*
Source: *Benson 2020 [11].*

Supplemental Appendix 2 – CD4 State Transition Probabilities

Table S4: Transition Probabilities - On Treatment, Viral Suppression (Weeks 0-48)

	TO					
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
From	**<50**	0.93	0.06	0.00	0.00	0.00
	50-199	0.02	0.92	0.06	0.00	0.00
	200-349	0.00	0.02	0.93	0.05	0.00
	350-500	0.00	0.00	0.02	0.93	0.05
	>500	0.00	0.00	0.00	0.01	0.99
**Viral load in copies/mL ^CD4 cell count in cells/mm3*						

Abbreviations: *CD4, cluster of differentiation 4*
Source: *NICE TA757 [2]*

Table S5: Transition Probabilities - On Treatment, No Viral Suppression (Weeks 0-48)

	TO					
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
From	**<50**	0.93	0.06	0.00	0.00	0.00
	50-199	0.02	0.92	0.06	0.00	0.00
	200-349	0.00	0.02	0.93	0.05	0.00
	350-500	0.00	0.00	0.02	0.93	0.05
	>500	0.00	0.00	0.00	0.01	0.99
	**Viral load in copies/mL ^CD4 cell count in cells/mm3*					

Abbreviations: *CD4, cluster of differentiation 4*
Source: *NICE TA757 [2]*

Table S6: Transition Probabilities - On Treatment, Viral Suppression (Weeks 49+)

	TO					
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
From	**<50**	0.88	0.11	0.00	0.00	0.00
	50-199	0.03	0.91	0.06	0.00	0.00
	200-349	0.00	0.03	0.92	0.05	0.00
	350-500	0.00	0.00	0.03	0.92	0.05
	>500	0.00	0.00	0.00	0.01	0.99
	**Viral load in copies/mL ^CD4 cell count in cells/mm3*					

Abbreviations: *CD4, cluster of differentiation 4*
Source: *NICE TA757 [2]*

Table S7: Transition Probabilities - On Treatment, No Viral Suppression (Weeks 49+)

	TO					
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
From	**<50**	0.88	0.11	0.00	0.00	0.00
	50-199	0.03	0.91	0.06	0.00	0.00
	200-349	0.00	0.03	0.92	0.05	0.00
	350-500	0.00	0.00	0.03	0.92	0.05
	>500	0.00	0.00	0.00	0.01	0.99
	**Viral load in copies/mL ^CD4 cell count in cells/mm3*					

Abbreviations: *CD4, cluster of differentiation 4*
Source: *NICE TA757 [2]*

Table S8: Transition Probabilities - Off Treatment

	TO					
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
From	**<50**	1.00	0	0	0	0
	50-199	0.01	0.99	0	0	0
	200-349	0	0.00	1.00	0	0
	350-500	0	0	0.01	0.99	0
	>500	0	0	0	0.00	1.00
	**Viral load in copies/mL ^CD4 cell count in cells/mm3*					

Abbreviations: *CD4, cluster of differentiation 4*
Source: Mangal et al. 2017 [1]

Supplemental Appendix 3 – Disaggregated Economic Results

Table S9: Economic model results – Base case assumptions

Cost	Standard of Care Cohort	Early Start Cohort	Incremental
ART costs	***$118,975,058***	***$119,767,278***	***$792,220***
Total health state costs	***$22,616,491***	***$22,554,243***	***-$62,248***
CD4: <50	$2,189,825	$2,158,509	-$31,316
CD4: 50-199	$3,260,442	$3,233,748	-$26,695
CD4: 200-349	$3,638,196	$3,608,067	-$30,128
CD4: 350-500	$3,579,389	$3,560,975	-$18,414
CD4: >500	$9,948,639	$9,992,944	$44,305
Total 3-year cost	***$141,591,549***	***$142,321,522***	***$729,972***
Deaths	27	26	-0.3
HIV transmissions	51	44	-7
Excess healthcare costs of new HIV transmissions	***$58,641,166***	***$50,409,399***	***-$8,231,767***

Abbreviations: *ART, antiretroviral therapy; CD4, cluster of differentiation 4; HIV: Human immunodeficiency virus.*

Table S10: Economic model results – Medicaid-covered population

Cost	Standard of Care Cohort	Early Start Cohort[a]	Incremental
ART costs	***$107,730,493***	***$111,440,966***	***$3,710,473***
Total health state costs	***$23,587,325***	***$23,273,047***	***-$314,277***
CD4: <50	$2,727,675	$2,556,706	-$170,969
CD4: 50-199	$3,646,376	$3,519,506	-$126,869
CD4: 200-349	$4,079,007	$3,934,447	-$144,560
CD4: 350-500	$3,822,735	$3,741,172	-$81,563
CD4: >500	$9,311,532	$9,521,216	$209,684
Total 3-year cost	***$131,317,817***	***$134,714,013***	***$3,396,196***
Deaths	31	30	-1.5
HIV transmissions	160	126	-34
Excess healthcare costs of new HIV transmissions	***$184,280,101***	***$145,175,889***	***-$39,104,212***

Abbreviations: *ART, antiretroviral therapy; CD4, cluster of differentiation 4; HIV: Human immunodeficiency virus.*

Footnotes: *[a]Rapid start defined as treatment within two weeks of diagnosis in this scenario.*

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