Online Supplementary Material

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This supplementary material has been provided by the authors to give readers additional information about their work.

Supplemental Appendix 1: CHEERS Checklist

Consolidated Health Economics Evaluation Reporting Standards 2022 (CHEERS 2022) Statement[1]

Section	Topic	Item No.	Guidance for Reporting	Reported in Section
Title	Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	Provided in title
Abstract	Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Manuscript abstract
Introduction	Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Lines 2-61
Methods	Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	N/A
	Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Lines 64-69
	Setting and location	6	Provide relevant contextual information that may influence findings.	N/A
	Comparators	7	Describe the interventions or strategies being compared and why chosen.	Lines 135-137, 152-160
	Perspective	8	State the perspective(s) adopted by the study and why chosen.	Line 66-67
	Time horizon	9	State the time horizon for the study and why appropriate.	Line 74-77
	Discount rate	10	Report the discount rate(s) and reason chosen.	Line 127-128
	Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Lines 67-69, 94-95, 108-110, 119-125

Section	Topic	Item No.	Guidance for Reporting	Reported in Section
Methods	Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Line 87-95, 108-112
	Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Line 94-95, 119-126
	Measurement and valuation of resources and costs	14	Describe how costs were valued.	Line 119-126, Table 1
	Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Table 1, Supplemental Appendix 2 (Table S7)
	Rationale and description of model	16	If modeling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Line 64-73
	Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	N/A
	Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	N/A
	Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	N/A
	Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis.	Line 165-177, 198-208, Table 5,
	Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	N/A
Results	Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Table 1-Table 4, Supplemental Appendix 2
	Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure.	Table 5
	Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	161-166, Table 6, Supplemental Appendix 3
	Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	N/A
Discussion	Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Line 211-292
Other relevant information	Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Included in cover letter
	Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Included in cover letter

Supplemental Appendix 2: Additional Model Inputs

Table S1. Transition Probabilities – On Treatment, Viral Suppression (Weeks 0-48)

		To				
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
	<50	0.93	0.06	0.00	0.00	0.00
	50-199	0.02	0.92	0.06	0.00	0.00
From	**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						

Abbreviation: CD4, cluster of differentiation 4.

Source: NICE TA757.[2]

Table S2. 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**
	<50	0.93	0.06	0.00	0.00	0.00
	50-199	0.02	0.92	0.06	0.00	0.00
From	**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/ mm^3						

Abbreviation: CD4, cluster of differentiation 4.

Source: NICE TA757.[2]

Table S3. Transition Probabilities – On Treatment, Viral Suppression (Weeks 49+)

		To				
Viral load*	**<50**					
CD4 cell count^		**<50**	**50-199**	**200-349**	**350-500**	**>500**
	<50	0.88	0.11	0.00	0.00	0.00
	50-199	0.03	0.91	0.06	0.00	0.00
From	**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/ mm^3						

Abbreviation: CD4, cluster of differentiation 4.

Source: NICE TA757.[2]

Table S4. 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						

Abbreviation: CD4, cluster of differentiation 4.

Source: NICE TA757.[2]

Table S5: Transition Probabilities – Off Treatment

		To				
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						

Abbreviation: CD4, cluster of differentiation 4.

Source: Mangal et al 2017.[3]

Table S6. Inputs Used to Model HIV Transmissions Arising from Heterosexual Men and Women, and Men Who Have Sex with Men, United States

Input	On Treatment	Off Treatment	Source
Per-act transmission probability			
Heterosexual men	0.0001	0.00159	
Heterosexual women	0.00021	0.00318	Supervie et al (2017)[4]
MSM	0.00134	0.01767	
Average risk acts per week	0.6209		Estrada et al (2022)[5]
Average weekly transmissions	**0.00059**	**0.00791**	**Calculation/CDC (2024)[6]**

Abbreviations: CDC, Centers for Disease Control and Prevention, MSM, men who have sex with men.

Table S7. Healthcare Cost Inputs Used to Model the Economic Consequences of a New HIV Infection in the United States

Input	Original Cost	Inflated Cost (Applied in Model)
Lifetime cost of HIV infection	$1,117,729 (2023)	$1,164,171
ART costs (per week)	$837.18 (2023)	$871.96
Health state costs (per week)		
CD4: <50	$842.41 (2017)	$966.62
CD4: 50-199	$378.09 (2017)	$433.83
CD4: 200-349	$202.61 (2017)	$232.48
CD4: 350-500	$143.51 (2017)	$164.67
CD4: >500	$106.71 (2017)	$122.44

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

Supplemental Appendix 3: Additional Sensitivity Analysis

Table S9 details results of supplemental scenario analyses conducted in addition to those presented in the main manuscript and which had a relatively minor impact on results. These scenarios explore the following:

- The proportion of individuals restarting treatment was increased by 10% in the rapid restart cohort.
- Alternate time horizons of 1 year and 5 years were applied to base case assumptions.
- Alternate waning periods for ART efficacy of 1 week and 5 weeks were applied to base case assumptions.
- The average probability of a non-virally suppressed individual transmitting an onward HIV infection was increased by 20%.
- The average lifetime cost of averting one HIV infection was increased by 20%.
- Transmission rates were updated to reflect annual transmission rates from a 2025 publication by the Centers for Disease Control and Prevention (CDC).[7] For this scenario, transmission rates were based on the following assumption:
  - Transmission rates for "Receiving HIV care (on ART) but not virally suppressed" applied when on treatment and not virally suppressed.
  - Transmission rates for "Aware and not in care" applied for individuals not on treatment and not virally suppressed.

The final scenario explored an updated baseline CD4 count distribution based on those published for a treatment interruption population[8]. A comparison of the base case CD4 distribution and these updated values are outlined in **Table S8**.

Table S8. Alternate CD4 Count Distribution

Scenario	Base Case Analysis[9,10]	Scenario[8]
CD4 <50	0.00%	11.7%
CD4 50-199	1.65%	22.1%
CD4 200-349	7.50%	23.6%
CD4 350-499	16.70%	16.4%
CD4 ≥500	74.15%	26.3%

Abbreviation: CD4, cluster of differentiation 4.

Table S9. Supplemental Scenario Analysis Results

Scenario	Inc. ART Costs	Inc. CD4 HS Costs	Inc. HIV Transmission	Inc. Costs from Averted Transmissions	Net Inc. Costs
Base case analysis	**$9,655,702**	**-$165,296**	**-88**	**-$101,083,857**	**-$91,593,451**
10% increase in restart proportion	$16,363,214	-$349,221	-151	-$171,365,793	-$155,351,801
Time horizon of 1 year	$9,635,592	-$58,081	-88	-$101,388,363	-$91,810,853
Time horizon of 5 years	$9,687,839	-$173,181	-88	-$100,810,390	-$91,295,732
ART waning of 1 week	$9,655,431	-$165,792	-88	-$101,084,889	-$91,595,250
ART waning of 5 weeks	$9,656,419	-$163,980	-88	-$101,081,713	-$91,589,274
20% increase in transmission probability	$9,655,702	-$165,296	-105	-$121,300,628	-$111,810,222
20% increase in lifetime HIV cost	$9,655,702	-$165,296	-88	-$121,300,628	-$111,810,222
Alternate source for transmission rates	$9,655,702	-$165,296	-12	-$13,712,892	-$4,222,487
Alternate source for baseline CD4 distribution	$10,358,040	-$1,844,424	-86	-$99,198,775	-$90,685,160

Abbreviations: ART, antiretroviral therapy; CD4, cluster of differentiation 4; HS, health state; Inc., incremental.

A probabilistic sensitivity analysis was also conducted. This involved assigning each variable in the model a relevant distribution which was then sampled for 1,000 iterations. A mean probabilistic result and associated 95% confidence interval was calculated for all outcomes.

Distributions were assigned according to the standard guidelines for probabilistic analysis in health economic modeling:[11]

- **Gamma** distribution assigned for costs
- **Beta** distribution assigned for binomial probabilities
- **Dirichlet** distribution used for multinomial probabilities or proportions
- **Normal** distribution applied for remaining parameters

Mean results over 1,000 iterations, as well as the corresponding 95% confidence intervals, are outlined in **Table S10.**

Table S10. Probabilistic Incremental Results (Mean and 95% CI) Over 1,000 Iterations

Category	Deterministic Results	Probabilistic Results	95% CI
Deaths	-0.184	-0.251	(-0.259, -0.243)
Transmissions	-87.88	-87.43	(-88.20, -86.66)
ART costs	$9,655,702	$9,693,089	($9,635,573, $9,750,604)
CD4 costs	-$165,296	-$159,593	(-$163,411, -$155,774)
Transmission costs	-$101,083,857	-$100,568,177	(-$101,447,047, -$99,689,307)

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

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