The Public Health and Economic Impact of Increased Screening and Early Initiation of Antiretroviral Treatment for HIV-1 in the UK

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BACKGROUND

- Early treatment of HIV-1 infection at all CD4 levels, rather than waiting for CD4 decline, has demonstrated substantial clinical benefits, including fewer AIDS- and non–AIDS-defining events.[1]
- Early treatment also prevents onward transmissions, as individuals with undetectable viral load do not transmit HIV to their partners.[2]
- Existing HIV screening efforts help facilitate earlier treatment, but a high proportion of individuals are still diagnosed late in the United Kingdom (UK).[3]
- Additional screening coupled with early treatment initiation could further reduce HIV-related morbidity, mortality, and transmission, but short-term costs for testing and treatment could increase.

OBJECTIVE

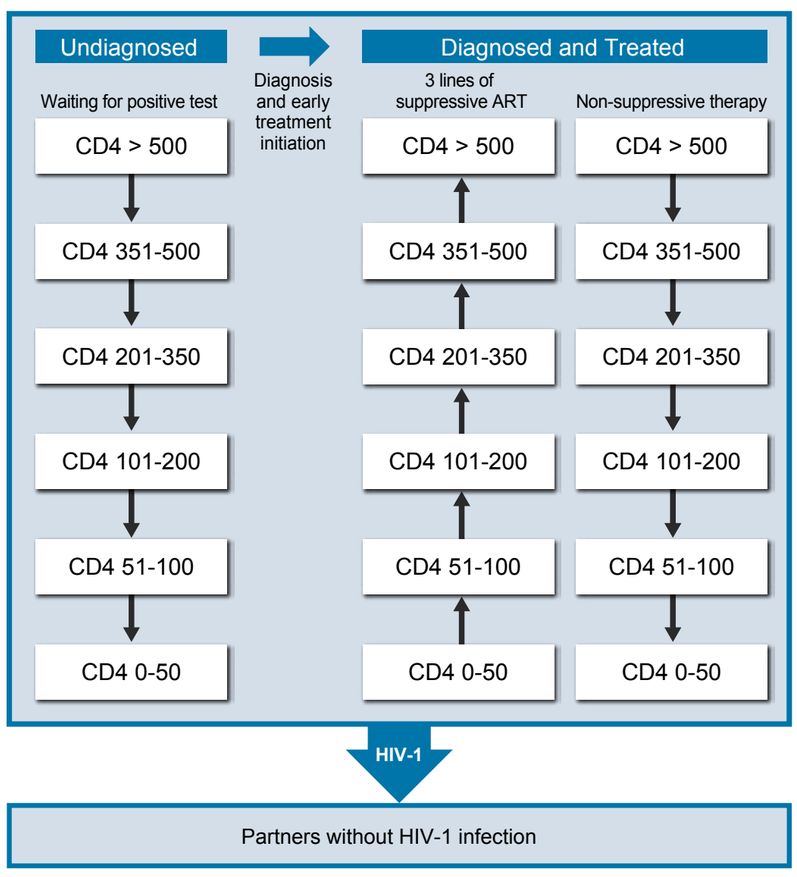
- This analysis examines the costs, health outcomes, and cost-effectiveness associated with increased HIV-1 screening and early initiation of treatment in the UK for men who have sex with men (MSM), heterosexuals, and people who inject drugs (PWID).

METHODS

Model Overview

- The Markov model followed theoretical cohorts of MSM, heterosexuals, and PWID with initially undiagnosed HIV-1 infection in the UK over their remaining lifetimes.
- The model examined increased HIV-1 screening (resulting in a 30% improvement in annual diagnosis rates) compared with current screening, with all individuals initiating early treatment within 3 months of diagnosis.
- In each 3-month cycle, individuals could remain in or transition between heath states (defined by CD4 cell count), move along the care pathway, or die due to causes related or unrelated to HIV (Figure 1).

Figure 1. Model Structure Diagram



In each cycle, all individuals were at risk of death due to causes related or unrelated to HIV.

- Before treatment initiation, individuals experienced declining CD4 cell count consistent with natural disease progression patterns.
- After treatment initiation, individuals progressed through up to four lines of antiretroviral therapy (ART), receiving recommended regimens typically used in the UK.
- As individuals progressed through the model, they incurred HIV screening and HIV-related clinical management costs and accrued quality-adjusted life-years (QALYs).
- Individuals were also at risk of transmitting HIV-1 infection to their partners according to a simple Bernoulli transmission model.[4]
- The model applied discounted lifetime costs and QALY losses to each secondary infection.

Table 1. Model Parameter Values, by Population Cohort

Parameter	MSM	Heterosexuals	PWID
Baseline characteristics: Individuals with undiagnosed HIV-1 infection[14]			
Mean age	35.9	39.6	37.8
Percentage male	100%	41%	81%
Annual change in CD4 count for untreated individuals, cells/µL[14,15]	–70.75	–72.50	–74.20
Transmission parameters (averages)			
Proportion of partners without HIV-1 infection[16]	94.10%	99.94%	99.12%
Long-term partners (before, after diagnosis)[17,18]	0.83, 0.66	0.79, 0.79	NA, NA
Unprotected interactions with long-term partners per cycle (before, after diagnosis)[19-21]	7.50, 3.53	17.02, 9.02	NA, NA
Number of years in long-term relationship[19]	1.5	1.5	NA
One-time partners/shared injections, unprotected, per cycle (before, after diagnosis)[18,22,23]	0.192, 0.090	0.005, 0.002	9.38, 4.41
Infectivity before ART initiation[16,24]	0.58%	0.089%	0.67%
Reduction in infectivity when on suppressive ART[2,23]	100%	100%	50%
Number of years presenting infection risk to others[19]	30	30	10
Costs and QALY losses			
Cost per positive test[25]	£5,000		
Average annual cost of ART (first line, second line, third line, nonsuppressive)[26]	£7,515, £7,937, £16,861, £23,564		
Discounted lifetime cost of managing a secondary HIV-1 infection[9]	£150,754		
Discounted total QALY loss for a secondary HIV-1 infection[9]	1.85		

NA = not applicable.

Table 2. Model Parameter Values for All Population Cohorts

Parameter	CD4 Cell Count (cells/µL)					
	> 500	351-500	201-350	101-200	51-100	0-50
Initial CD4 cell count distribution at baseline[14]						
MSM	41%	25%	18%	7%	4%	6%
Heterosexuals	22%	18%	22%	16%	8%	15%
PWID	21%	19%	21%	19%	13%	8%
3-month cost of HIV-related clinical management (not including ART)[27]						
When untreated	£811	£811	£811	£1,884	£1,884	£1,884
When treated	£1,268	£1,268	£1,268	£2,003	£2,003	£2,003
Utility value[28]	0.946	0.933	0.931	0.853	0.853	0.781

Input Parameters

- Clinical and behavioural characteristics of the cohorts entering the model and over time were based on UK-specific surveillance data and published literature (Table 1, Table 2).
- Efficacy and duration of first-, second-, and third-line ART regimens were taken from published observational studies and clinical trials (data not shown).[5-9]
- In the fourth, non-suppressive line of therapy, individuals experienced a steady decline in CD4 cell count (–22 cells/µL annually) until death.[10]
- HIV screening costs, HIV-related clinical management costs, and utility values were taken from published literature (Table 1, Table 2).
- HIV-related and non–HIV-related mortality rates and were taken from published literature and standard sources for the UK (data not shown).[11-13]
- Lifetime costs and QALY losses incurred by partners with a secondary HIV-1 infection were derived from published literature (Table 1).

RESULTS

- Increased HIV-1 screening followed by early treatment initiation resulted in fewer years undiagnosed, more years with CD4 cell counts above 200 cells/µL, more QALYs, and fewer HIV transmissions per person for all patient cohorts (Table 3).
- Incremental cost-effectiveness ratios for heterosexuals were within typical UK willingness-to-pay thresholds and were well below these thresholds for MSM and PWID (Table 3).
- Deterministic one-way sensitivity analysis showed that model results were robust.

Table 3. Base-Case Results[a]

Outcome	MSM		Heterosexuals		PWID	
	Current	Increased Screening	Current	Increased Screening	Current	Increased Screening
Years spent undiagnosed	0.99	0.59	1.89	1.42	0.74	0.37
Years with CD4 cell counts > 200 cells/µL	17.72	18.16	13.96	14.87	16.25	16.92
QALYs[b]	17.67	17.97	15.00	15.68	16.73	17.19
Onward transmissions per 100 individuals with HIV-1 infection	35.69	31.37	16.75	15.12	68.16	62.05
Total costs[b]	£378,748	£382,561	£295,967	£311,569	£413,966	£417,834
Incremental cost per QALY gained	£9,874		£21,908		£6,726	

[a] All outcomes are per-person averages and discounted at an annual rate of 3.5% unless otherwise noted.[29]
[b] Costs and QALYs included those accrued by the initial model cohort and by any of their partners with a secondary HIV-1 infection. Costs are presented in 2017 UK pounds.

LIMITATIONS

- The transmission model did not account for onward transmission beyond secondary infections and therefore provides conservative estimates of the benefits of increased screening and early treatment initiation.
- Data for several of the model parameters were somewhat dated. However, sensitivity analyses showed that model results were relatively insensitive to likely shifts in these parameters over time.

REFERENCES

See handout for references.

CONCLUSION

- Increased HIV-1 screening and early treatment initiation may be a cost-effective strategy to reduce HIV transmission and improve health for MSM, heterosexuals, and PWID in the UK.

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REFERENCES

1. Lundgren JD, Babiker AG, Gordin F, et al. N Engl J Med. 2015 Aug 27;373(9):795-807.
2. Rodger AJ, Cambiano V, Bruun T, et al. JAMA. 2016 Jul 12;316(2):171-81.
3. Public Health England (PHE). Health Protection Report Advanced Access Report [v2]. 2018 Sep 4;12(32):1-5.
4. Pinkerton SD, Abramson PR. In: Holtgrave DR, editor. Handbook of Economic Evaluation and HIV Prevention Programs. New York: Plenum Press; 1998: 13-32.
5. Arribas JR, Pozniak AL, Gallant JE, et al. J Acquir Immune Defic Syndr. 2008 Jan; 47(1): 74-8.
6. Beck EJ, Mandalia S, Lo G, et al. PLoS ONE. 2011 May; 6(5): e20200.
7. Mocroft A, Phillips AN, Ledergerber B, et al. Poster at the 9th International Congress on Drug Therapy in HIV Infection; November 9-13, 2008; Glasgow, Scotland.
8. Beck EJ, Mandalia S, Youle M, et al. Int J Std AIDS. 2008 May; 19(5): 297-304.
9. Yazdanpanah Y, Sloan CE, Charlois-Ou C, et al. PLoS ONE. 2010 Oct;5(10):e13132.
10. Ledergerber B, Lundgren JD, Walker AS, et al. Lancet 2004: 364(9428): 51-62.
11. Phillips AN, Gazzard B, Gilson R, et al. AIDS. 2007 Aug 20;21(13):1717-21.
12. Lewden C, Bouteloup V, De Wit S, et al. Int J Epidemiol 2012. Apr; 41(2): 433-45.
13. Office for National Statistics. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathregistrationssummarytablesenglandandwalesreferencetables.
14. PHE, HIV/AIDS New Diagnoses Team, HIV and STI Department, London, United Kingdom. Custom data analysis. 2014
15. Phillips AN, Lampe FC, Smith CJ, et al. AIDS. 2010 Jun 19;24(10):1561-7.
16. Cresswell F, Waters L, Briggs E, et al. Int J STD AIDS. 2016 Aug;27(9):713-38.
17. Camoni L, Dal Conte I, Regine V, et al. Ann Ist Super Sanita 2011; 47(2): 214-219.
18. Robinson C, Nardone A, Mercer C, Johnson AM. https://digital.nhs.uk/catalogue/PUB03023. Accessed February 7, 2018.
19. Xiridou M, Geskus R, de Wit J, Coutinho R, Kretzshmar M. AIDS. 2003 May;17(7):1029-38.
20. Johnson AM, Mercer CH, Erens B, et al. Lancet. 2001 Dec;358(9296):1835-42.
21. Marks G, Crepaz N, et al. J Acquir Immune Defic Syndr. 2005 Aug;39(4):446-53.
22. Hickson F, Bourne A, Weatherburn P, Reid D, Jessup K, Hammond G. 2010. Available at: http://sigmaresearch.org.uk/files/report2010b.pdf. Accessed February 7, 2018.
23. Long EF, Brandeau ML, Galvin CM, et al. AIDS. 2006 Nov;20(17):2207-15.
24. Benn P, Fisher M, Kulasegaram R, et al. Int J STD AIDS. 2011 Dec;22(12):695-708.
25. Health Protection Agency. 2011. http://www.bhiva.org/documents/Publications/ Time_to_test_final_report__Sept_2011.pdf.
26. MIMS. Available at: https://www.mims.co.uk/. Accessed: January 31, 2018.
27. Beck EJ, Mandalia S, Sangha R, et al. PLoS ONE. 2011 Dec;6(12):e27830.
28. Simpson KN, Luo MP, Chumney E, Sun E, Brun S, Ashraf T. HIV Clin Trials. 2004;5(5):294-304.
29. NICE. Available at: https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781. Accessed February 6, 2018.