



JOHNS HOPKINS
MEDICINE

Economic and epidemiologic impact of early ART initiation in Spain

**Parastu Kasaie¹, Sunaina Kapoor³, Matthew Radford², David Dowdy¹, Maunank Shah³,
1. Johns Hopkins Bloomberg School of Public Health,
2 ViiV Healthcare,
3. Johns Hopkins School of Medicine**

Introduction

- ART initiation has been shown to decrease HIV transmission
- Data from the START trial and others suggests that early ART initiation (irrespective of CD4 count) may reduce the rates of AIDS and non-AIDS events and death
- European and other international guidelines now recommend ART initiation irrespective of CD4 count
- Early ART initiation may decrease transmission and morbidity and mortality, but could increase costs
- The population level impact of guidelines for early ART initiation on costs, incidence, and outcomes has not been fully quantified

Objectives

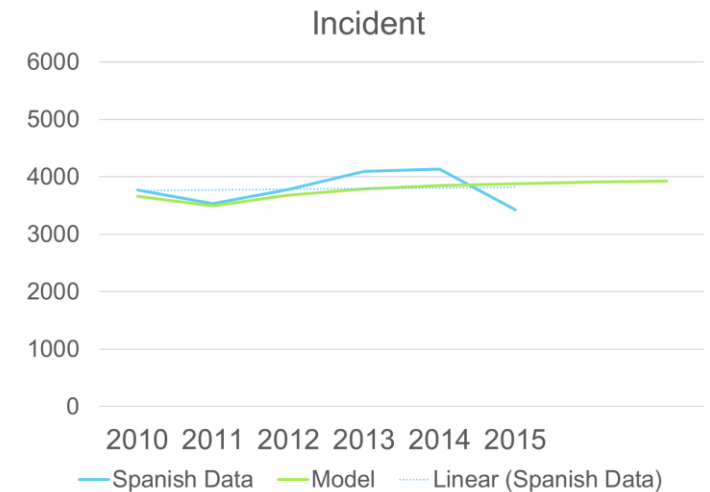
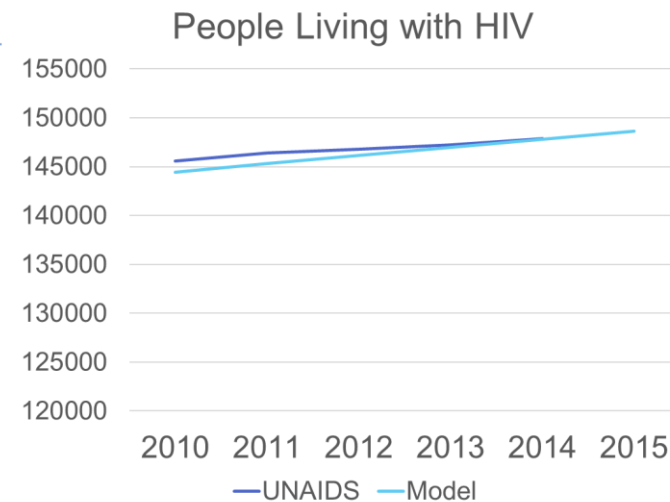
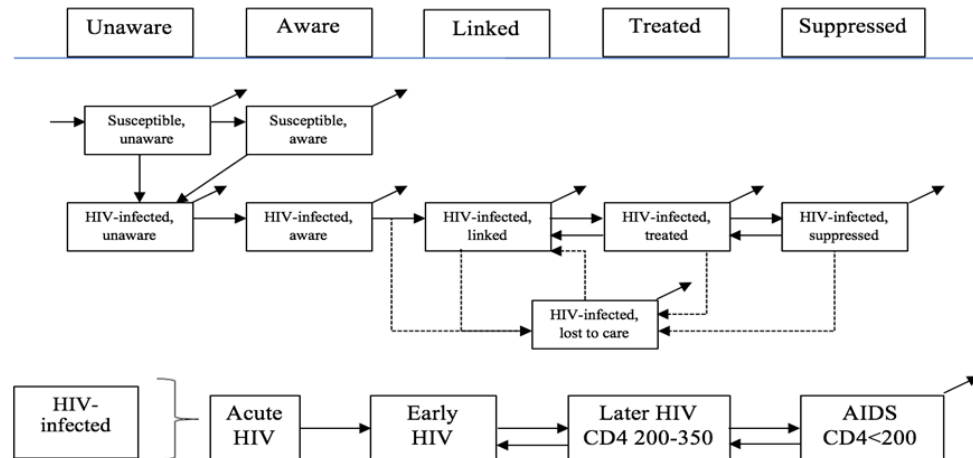
- To quantify the epidemiologic and economic impact of early ART (and CD4 count) initiation compared to a counterfactual scenario of delayed ART (at CD4 <350) in Spain over 20 years
- Primary Outcomes:
 - Total health system costs
 - Incident cases averted (%)
 - HIV/AIDS deaths averted (%)
 - Events (AIDS and non-AIDS) averted (%)
 - QALY's gained
 - Incremental cost-effectiveness ratio
- Secondary Outcomes:
 - Impact of the HIV care continuum on early ART initiation

METHODS

Study Design: mathematical modeling analysis using The **Johns Hopkins Economic Epidemiologic model**

Modeling approach:

- We model sexual and injection drug use transmission, along with HIV natural history and care engagement among (age-stratified) heterosexuals, MSM, and injection drug users
- Costs were collected based on literature estimates from Spain, and accumulate based on utilization in the model
- Model Calibration to observed epidemiology from Spanish surveillance sources, and UNAIDS¹



1. Partial list of sources for calibration and epidemiology of HIV in Spain included:

a)UNAIDS. AIDSinfo 2016. Available from: <http://aidsinfo.unaids.org/>.

b)National Center for Epidemiology. Mortality by HIV and AIDS in Spain, year 2014.

c)National Center for Epidemiology. Epidemiological Surveillance of HIV and AIDS in Spain: Information System on New HIV Diagnoses and National Registry of AIDS Cases. 2016.

d)-European Centre for Disease Prevention and Control. HIV/AIDS surveillance in Europe 2015. Available from: <https://ecdc.europa.eu/en/publications-data/hivaids-surveillance-europe-2015>

Model inputs

Parameter	Base-case value	Range
ART costs (average of GESIDA 2017 first-line) ¹	€8600	€6435-22180
Labs: HIV test, Genotype, viral load, CD4,HLAB5701 ²	€19-350 depending on lab test	
Office visit	~€100	€50-250
Cost AIDS events (weighted average of TB, lymphoma, Kaposi Sarcoma, pneumocystis) ³	€19000	€9500-100,000
Cost non-AIDS events ³ (weighted average of MI, CVA, other malignancies)	€9700	€5000-17000
AIDS events rate (increased for lower CD4 counts) ³	.0072	.005-.01
Non-AIDS event rate (increased for lower CD4) ³	.0067	.005-.01
Hazard ratio with ART (AIDS events) ³	0.28	.015-0.5
Hazard ratio with ART (non-AIDS events) ³	0.61	0.38-0.97
Relative risk reduction of AIDS death with ART	95%	50%-98%

1. Costs based on first line ART recommendations (<http://gesida-seimc.org/category/guias-clinicas/antirretroviral-vigentes/>), and based on published cost estimates: *Rivero et al. Costs and Cost-efficacy analysis of 2017 GESIDA recommended guidelines for initial ART in HIV-infected adults. Enferm Infecc Microbiol Clin 2017.*

2. Laboratory costs for HIV screening, as well as longitudinal care were included and based on literature estimates

3. Event rates and ART effects were based on START Trial (NEJM 2015; 373(9):795-807); we used literature estimates from Spain for costs of various AIDS and non-AIDS events, and utilized a weighted average based on specific event rates in START trial.

**Not all model parameters and references are shown. Additional literature sources were used to estimate ranges, utility weights, care continuum parameters, population sizes and others. Transmission parameters were calibrated to the observed epidemiology for incidence, prevalence, deaths, and care continuum in Spain*

Results:

Economic and Epidemiologic Impact of Early ART over 20 years

Strategy	Incident Cases	Events (AIDS and non-AIDS)	Excess Deaths	Total Health System Costs	QALY's	ICER	%Suppressed
Delayed ART (CD4<350)	85,800	91,400	29,700	€17.28 billion	REF	REF	57%
Early ART	64,300	80,800	26,000	€18.13 billion			65%
Incremental (Δ) ^{1,2}	21500 cases averted (25% reduction)	10,700 events averted (12% reduction)	3670 deaths averted (12% reduction)	€842 million ³	29,640 per QALY gained ³	€28,400 per QALY gained ⁴	8%

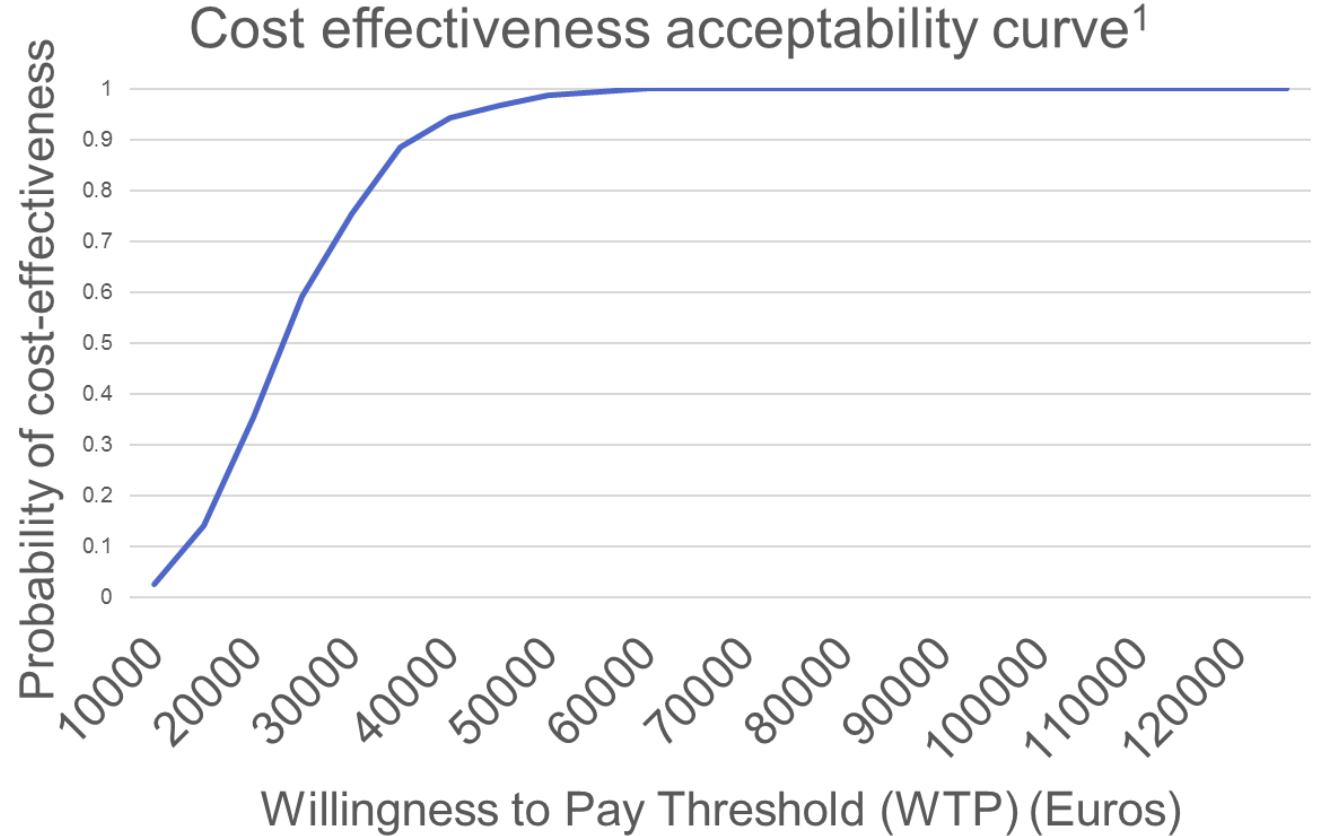
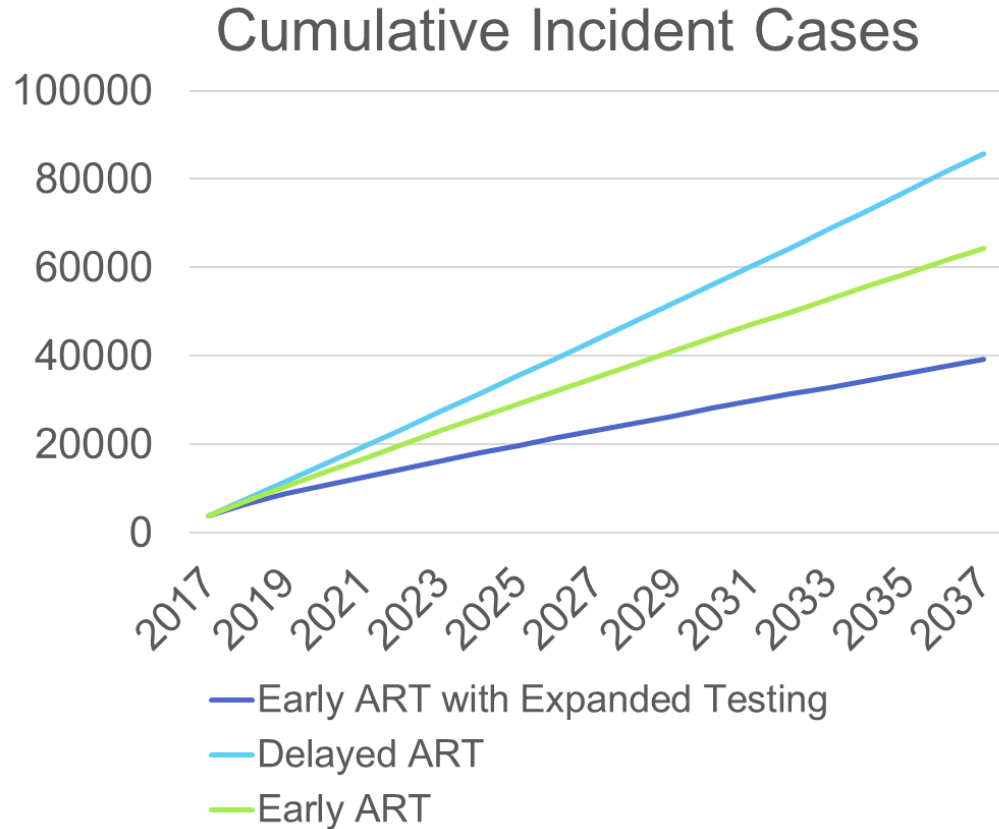
1. When examining a 30 year time horizon, early ART results in a 28% reduction in incidence, at an incremental cost of €733 million, and an ICER of €11,000 per QALY gained.
2. When examining a 40 year time horizon, early ART results in a 31% reduction in incidence, at an incremental cost of €370 million, and an ICER of €3200 per QALY gained.
3. Future costs and QALY's are discounted at 3%
4. One-way sensitivity analysis: ICER is €18,500 to €43,000 per QALY-gained for annual ART costs ranging €6000 to €12,500 per year

Results: Economic and Epidemiologic Impact of Early ART Plus Annual Testing of high risk groups over 20 years

Strategy	Incident Cases	Events (AIDS and non-AIDS)	Excess Deaths	Total Health System Costs	QALY's	ICER	% Suppressed
Delayed ART (CD4<350)	85800	91400	29700	€17.28 billion	REF	REF	57%
Early ART+ annual high risk testing ¹	39178	61,200	16,400	€20.3billion			72%
Incremental (Δ)	46,600 cases averted (54% reduction)	30,300 events averted (33% reduction)	13,300 deaths averted (44% reduction)	€3.02 billion	106,900 per QALY gained	€28,200 per QALY gained	15%

1. Includes the cost of an annual HIV test (€19) to MSM, young heterosexuals, and people with injection drug usage; no ancillary program costs were included in base-case

Results



1. In probabilistic sensitivity analysis, all parameters were varied randomly across their ranges. The probability that the ICER is lower than different WTP thresholds is shown. At WTP of €30,000 per QALY gained, 75% probability of being cost-effective compared to delayed ART

Conclusions

- Recommendations for early ART initiation are highly cost effective at a willingness to pay threshold of €30000/QALY-gained
- Without early ART initiation, there would be over 25% more new cases in Spain over 20 years
- Coupling early ART initiation with improved testing (i.e. improving HIV diagnosis) could reduce cumulative incidence by half over 20 years
- In Sensitivity Analysis, the cost-effectiveness is most influenced by the cost of ART

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