European Journal of Public Health, 2025, ckaf057

https://doi.org/10.1093/eurpub/ckaf057

Estimating the potential health economic value of introducing universal opt-out testing for HIV in emergency departments in Italy

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Abstract

In Italy, an estimated 13 000–15 000 people have undiagnosed HIV, and in 2020, 60% of new diagnoses were late-stage (CD4 < 350 cells/mm^3). In hospitals, including emergency departments (EDs), testing is largely limited to indicator-condition-guided testing (IC), with written consent universally required. We developed a closed-cohort hybrid decision tree–Markov model to compare health economic values of two HIV testing strategies in the ED: (1) universal opt-out and (2) IC (Italian standard of care). Data sources included healthcare costs and HIV public health data, obtained from national reports and published studies. A lifetime time horizon and a National Health Service perspective were used. Primary outcomes were life years, quality-adjusted life years (QALYs), and costs. Universal opt-out testing resulted in better health outcomes at higher costs. For every 10 000 individuals attending ED, opt-out testing resulted in 15.78 additional new HIV diagnoses and 14.47 more people linked to HIV care compared with IC. Prevalence threshold analysis demonstrated that opt-out testing was cost-effective compared to IC when the HIV prevalence was 0.25% or higher, assuming a willingness-to-pay threshold of €30 000/QALY. Universal opt-out HIV testing in the ED could be a cost-effective way to increase the number of new HIV diagnoses and improve HIV health outcomes in Italy. The model may underestimate the full benefits of this strategy as our model did not consider disengaged patients or transmissions averted. Further research using real-world data is needed to verify our findings.

Introduction

Treatment for human immunodeficiency virus (HIV) has improved to the point where people living with HIV (PLWH) who are on antiretroviral therapy (ART) with an undetectable viral load have a normal life expectancy and cannot transmit the virus [1]. However, late diagnosis of PLWH (CD4 < 350 cells/mm^3) is associated with higher morbidity and mortality, a greater risk of transmission and increased healthcare costs [2, 3].

In Italy, the annual number of new diagnoses has been declining since 2012, but the proportion of late diagnoses has increased, reaching 60% in 2020—10% higher than the European average [4]. While sex between men remains the primary transmission route, the proportion of late-stage diagnoses is higher among self-reported heterosexual people, particularly men over 40 [4]. The proportion of new cases among young people (ages 25–39) has decreased, while cases among people over 50 have increased [4].

In Italy, at the time of writing, written consent is required for HIV testing (i.e. opt-in) except for antenatal screening, which is opt-out (i.e. all individuals are screened unless the patient declines/opts out) [5]. HIV testing in routine healthcare settings including emergency departments (EDs), and inpatient units, is largely limited (and inconsistently implemented) to individuals presenting with HIV-indicator conditions [6–8]. With an estimated 13 000–15 000 undiagnosed HIV cases in Italy and high late-stage diagnoses, innovative testing strategies are needed to make progress towards achieving the UNAIDS HIV target of diagnosing 95% of PLWH [4, 9].

EDs are a key touch point with the healthcare system for marginalized groups and people who may not routinely use sexual health services [10]. The European Centre for Disease Prevention and Control (ECDC) guidance in 2010 mentions ED HIV testing within broader testing strategies, particularly in high-prevalence settings [11]. However, such strategies have not been widely adopted into national guidelines [11, 12], except recently for England, where blood-borne virus (BBV) opt-out testing in EDs covering high-prevalence areas has been part of the national action plan since 2022 [13]. Opt-out testing results in higher uptake than opt-in strategies for BBV testing in EDs [10]. The cost-effectiveness of opt-out testing increases in populations with high incidence, test acceptance rates, and large proportions of individuals unaware of their infection [14]. Recent studies from England, Ireland, and Portugal have demonstrated the real-world clinical effectiveness (increased number of diagnoses and patients linked to care) of universal opt-out ED testing strategies in medium/high-prevalence regions [15–18]. Furthermore, evidence from England suggests that this strategy is more effective for diagnosing heterosexuals and black minority ethnic individuals than traditional client-initiated testing [13, 15]. In Italy, a formal legal review of HIV testing legislation (requiring

written patient consent) is currently underway. This study aimed to contribute to the informed national dialogue by evaluating the potential health economic value of introducing a universal opt-out HIV testing strategy in EDs in Italy.

Methods

A closed-cohort hybrid decision tree–Markov model was developed in Excel® 2021 (Microsoft, Redmond, WA) to compare two ED-based HIV testing strategies: (1) universal opt-out testing versus (2) indicator-condition guided testing (IC), the current standard of care (SoC) in Italy.

The opt-out testing algorithm simulated in the model was based on recent real-world evidence studies [15–18]. The natural history of disease element was based on prior modelling studies of ART treatment [19, 20] and practice informed by clinical guidelines [21]. Italian clinical experts verified the model's design to ensure its validity and accuracy for current and expected clinical practice in Italy.

The model simulated a cohort of 10 000 ED attendees who required a blood test as part of their ED visit. The model used a lifetime time horizon and took the perspective of the Italian National Health Service. The model's primary outcomes were the incremental total life years, QALYs, costs, and costs-per-QALY. Future health benefits and costs were discounted by 3% annually according to Italian Medicines Agency guidelines [22].

The study was conducted and reported using the CHEERS checklist [23]. An ethics review was not sought as all data were publicly available, and no patient-identifying data were used.

Model design

The model used a decision tree structure to characterize the outcomes following the initial ED visit and a Markov model to characterize the longer-term outcomes for individuals simulated in the model [19].

Initial ED visit: universal opt-out HIV testing

The steps involved in universal opt-out HIV testing simulated in the model were informed by real-world examples from other countries [16, 17] and are present in Fig. 1A. Initially, an automated electronic patient record (EPR) system triggers an HIV-1 test request for all adult ED attendees requiring a blood test. If the patient does not opt-out, their blood sample is tested using a fourth-generation antibody/antigen test followed by a Western blot confirmatory test in accordance with Italian diagnostic guidelines. With sensitivity and specificity exceeding 99%, the model considers these tests as 100% accurate [24]. Individuals who test negative (screening or confirmatory) are excluded from the model beyond this point. Individuals who test positive are categorized into new or prior diagnoses. The model assumes that everyone newly diagnosed is then linked to HIV care (LTC) which comprises four steps: (1) test result notification, (2) initial consultation scheduling, (3) initial treatment consultation, and (4) ART initiation. The model did not consider changes in clinical management for individuals previously diagnosed.

Initial ED visit: IC testing

The model assumes that people attending the ED with an HIV-indicator condition (an opportunistic infection, OI) are tested for HIV. The proportion of attendees with an OI was calculated using monthly event probabilities among HIV-positive individuals (see Supplementary Material S1). The model assumed the same diagnostic testing and LTC protocols for IC testing as for universal opt-out testing.

Long-term outcomes

In line with ART treatment modelling studies, the health states used in the Markov model were based on both ART regimen and immunologic status [19]. Five treatment states were simulated: off-treatment, three active ART states (representing 1st, 2nd, and 3rd line treatment regimens), and a salvage ART regimen state. Each of the five treatment states had four CD4 substates (<200, 200–<350, 350–<500, and ≥500 cells/mm^3) (Fig. 1B). Death was the absorbing state. The Markov model used a one-month cycle length. A treatment algorithm was implemented to manage assignment to ART regimens across treatment lines based on reasons for discontinuation (Supplementary Fig. S1). For both testing strategies, the initial treatment assignments of the modelled cohort were determined by testing and LTC outcomes from the initial ED visit: (1) new diagnosis, LTC: on ART; (2) new diagnosis, not LTC: off-treatment; (3) undiagnosed, off-treatment. After entering a treatment state, individuals progress through the CD4 states and improve, remain stable, or decline. The rate of transition between CD4 states was governed by treatment-related transition probabilities. Virological response rates (<50 copies/ml) were incorporated into ART regimen discontinuation probabilities. Individuals not receiving treatment were assumed to experience continuous immunological decline. All individuals, regardless of state, were assumed to be at some risk of OIs (Supplementary Material S1 provides further details). QALY estimates were based on utility values for each CD4 state and utility decrements for OI events.

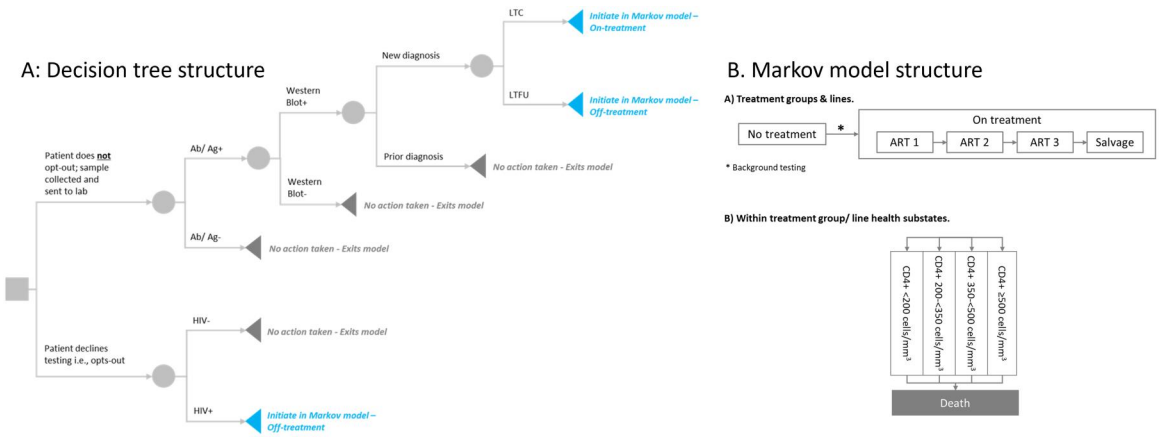

Figure 1. Universal opt-out ED testing algorithm decision tree (A) and Markov model schematic (B). Abbreviations: Ab/Ag: antibody/antigen; ART: antiretroviral therapy; HIV: human immunodeficiency virus; LTC: linked to care; LTFU: lost to follow-up.

Model inputs

Initial ED visit

There is no systematic HIV testing in EDs in Italy, and there were no data on HIV prevalence among ED attendees in Italy. Thus, evidence from other European studies, confirmed with Italian authors for suitability, was used to inform the input variables for the universal opt-out testing strategy and the cohort's HIV prevalence. The main analysis reported here predominantly used data from a Portuguese study [17], the largest currently published study on universal opt-out ED HIV testing in Europe (252 153 ED visits). It evaluated the impact of a three-year automated EPR-based screening programme in the ED in a medium-high HIV prevalence setting (0.52%). The programme used a sophisticated EPR algorithm to automatically exclude previously diagnosed individuals. This study was selected to inform the primary analysis as it was considered the most complete published evaluation. A secondary analysis was run using data from a service evaluation [16] which assessed the nine-month implementation of a routine opt-out ED BBV testing programme in a medium prevalence setting in England (representing 112 479 ED visits and an HIV prevalence of 0.41%). As well as HIV prevalence, the proportion of new diagnoses among positive cases and the opt-out rate differed between these two studies, the latter likely due to different ERP models.

The costs for the ED visit included HIV testing costs and LTC, covering both administrative time and treatment consultation. All inputs used for the ED visit are present in Table 1.

Baseline characteristics. Characteristics (age and CD4 count) of PLWH presenting to EDs in Italy are unknown. Therefore, national-level data were used from the Istituto Superiore di Sanitá report on HIV diagnoses & AIDS cases. In 2022, the mean age of people with a new HIV diagnosis was 45.8 years, and 58.1% had CD4 < 350 cells/mm (as measured at point of entry to HIV care) [3, 4].

Long-term outcomes

Disease and treatment outcomes. Mean CD4 count change values and cause-specific discontinuation probabilities associated with each regimen are provided in Supplementary Table S2. The ART 1 regimen outcome profile was based on ART regimens used for 1st line management of treatment naïve PLWH in Italy. Specifically, outcome data for individual ART regimens were weighted by their relative market share, which was informed by Italian national-level data. Outcomes of ART regimens were based on clinical trial reporting. Outcome data for the ART 2, 3, and salvage treatment states were derived from established technology appraisals [27]. For the no-treatment state, a continual decline in CD4 count was modelled. See Supplementary Material S2 for further explanation and sources used.

Background HIV testing. For both testing strategies, the model assumes that if someone with HIV does not initiate treatment shortly after their ED visit (they are either undiagnosed or diagnosed but not LTC) they can subsequently be diagnosed and start treatment. The probability that they will subsequently be tested for HIV (referred to as background HIV testing) was based on a combination of the annual probability that they test (informed using data from the Piemonte region [28] in the absence of data from Italy) and the probability of an OI event (dependent on CD4 health state) informed by d'Arminio Monforte *et al.* [25] (Supplementary Table S9).

Opportunistic infections, mortality, and utilities. OI event probabilities were derived by aetiology, CD4 state, and time since treatment initiation [25] (Supplementary Table S5).

Health state-specific mortality probabilities were determined using Italian general population mortality data combined with CD4 count-standardized mortality ratios (Supplementary Table S6).

Supplementary Table S7 provides the utilities used for each CD4 state and the OI event utility decrements.

Costs. Supplementary Table S8 summarizes long-term outcomes costs, including ART costs by treatment line, outpatient services, non-ART medication, hospitalizations, and end-of-life care. All costs were inflated to 2022 using the Consumer Price Index for health goods [29]. ART costs were estimated from Italy's regimen market share data. In line with prior modelling studies for Italy [30], individual ART drug treatment costs were obtained from the latest (2021) Lombardy report on HIV/AIDS care [31]. The treatment naïve market share data were used to estimate ART 1 regimen profile costs, while the switch share data, representative of 2nd line treatment, were used for ART 2 and ART 3 regimen profiles. Salvage treatment line regimen profiles were estimated relative to the ART 1 profile. On- and off-treatment states assumed profiles for undetectable (<50 copies/ml) and detectable viral loads (≥50 copies/ml), respectively. Only hospitalization, end-of-life care, and non-highly active ART costs were considered for the off-treatment state. OI event costs were assumed to be captured within the hospitalization costs. End-of-life care costs were added in the last three months before death. Background HIV testing and LTC costs in the Markov model are the same as those in the ED visit

Scenario analyses

Given the significant data gaps, several scenarios were assessed using the primary input profile (i.e. informed Vaz-Pinto *et al.* [17]). Supplementary Table S10 contains further details.

(1) A threshold analysis was conducted to determine the minimum HIV prevalence at which universal opt-out testing would be cost-effective compared to IC testing. ED HIV prevalence values ranging from 0.15% to 1.20% were assessed, drawing on data from similar interventions in Europe and Canada (sources detailed in Supplementary Table S11).
(2) Analyses assessing the impact of different patient characteristics (i.e. age and CD4 count at diagnosis).
(3) A scenario where IC testing was based on OI events only (i.e. did not include testing for other reasons).
(4) A scenario using a lower rate of LTC following diagnosis (58.00% compared to 91.67% in the main analysis) informed by opt-out BBV testing in 34 EDs in high HIV prevalence areas in England [18].

Sensitivity analyses

One-way sensitivity analyses were performed to evaluate how changes in input values affect the results and to identify the most influential parameters. Individual parameters or parameter groups were varied by ±20% deviation from the mean. The primary input profile was used for sensitivity analyses [17].

Results

Primary analysis

When HIV prevalence among ED attendees was 0.52%, as informed by Vaz-Pinto *et al.* [17], for every 10 000 attendees, universal opt-out testing resulted in 15.78 additional new HIV diagnoses (15.99 vs. 0.21) and 14.47 more individuals linked to care (14.66 vs. 0.19). Universal opt-out testing resulted in increased life years and QALYs at a higher cost than IC testing and the ICER for the universal opt-out testing was €24 680/QALY.

Table 1. Model input parameters used for the initial ED visit

Inputs used in primary analysis			
Parameter group	**Parameter**	**Value**	**Source**
Prevalence and participation	HIV prevalence in ED attendees	0.52%	Vaz-Pinto *et al.* [17]
	Percentage of HIV-positive people undiagnosed at start of ED attendance	34.67%	
	Number of HIV-positive people undiagnosed at start of ED attendance	17.99	Calculated: 10 000 × 0.52% × 34.67%
	Percentage of people tested during ED visit in universal opt-out testing strategy	88.89%	Vaz-Pinto *et al.* [17]
	Percentage of people tested during ED visit in indicator-condition guided testing	1.16%[a]	D'Arminio Monforte *et al.* [25]
	Percentage of people with new HIV diagnosis who are then linked to HIV care (including treatment initiation)	91.67%[b]	Smout *et al.* [16]
Inputs used in secondary analysis			
Parameter group	**Parameter**	**Value**	**Source**
Prevalence and participation	HIV prevalence in ED attendees	0.41%	Smout *et al.* [16]
	Percentage of HIV-positive people undiagnosed at start of ED attendance	17.14%	Smout *et al.* [16]
	Number of HIV-positive people undiagnosed at start of ED attendance	7.09	Calculated: 10 000 × 0.41% × 17.14%
	Percentage of people tested during ED visit in universal opt-out testing strategy	60.05%	Smout *et al.* [16]
	Percentage of people tested during ED visit in indicator-condition guided testing	1.16%[a]	D'Arminio Monforte *et al.* [25]
	Percentage of people with new HIV diagnosis who are then linked to HIV care (including treatment initiation)	91.67%	Smout *et al.* [16]
Inputs used in primary and secondary analyses			
Parameter group	**Parameter**	**Value**	**Source**
Costs (for year 2022)	Fourth generation Ab/Ag HIV test [Screening]	22.70€	Lombardia Nomenclatore Tariffario 2022 [26]
	Western blot test [Confirmatory]	100.29€	
	Supplementary Table S1 includes healthcare costs associated with nurse time and linkage to HIV care		See Supplementary Table S1
Profile of HIV positive ED presenters	Baseline age (years)	45.83[c]	ISS, 2022 HIV and AIDS case diagnosis report—National level profile [4]
	Proportion female	20.90%	
	Baseline CD4 cell count (cells/mm^3) proportional distribution		
	<200	40.65%	ISS, 2022 HIV and AIDS case diagnosis report—National level profile [4]
	200–<350	17.49%	
	350–<500	17.16%	
	≥500	24.70%	

a: A percentage of undiagnosed HIV-positive individuals were assumed to present with OIs and to undergo indicator-condition testing. The percentage of individuals presenting with OIs was based on AIDS event risks derived from d'Arminio Monforte *et al.* [25].
b: The percentage of patients initiating treatment was based on Smout 2022 [16] reporting as these data were not available from the Vaz-Pinto 2022 [17] study—91.67% of new diagnoses initiated treatment within six months.
c: Derived by weighting mid-point of reported age categories by associated *n* values.
Abbreviations: Ab: antibody; Ag: antigen; ART: antiretroviral therapy; ED: emergency department; HIV: human immunodeficiency virus; LTC: linkage to care; OI: opportunistic infection.

Secondary analysis

In the secondary analysis, when data inputs were informed by Smout *et al.* [16], at an HIV prevalence of 0.41%, for every 10 000 people presenting to the ED, universal opt-out testing resulted in 4.18 additional new diagnoses (4.26 vs. 0.08) and 3.83 more individuals LTC (3.90 vs. 0.08) compared with IC testing. In this analysis, the ICER was €32 220/QALY. HIV threshold analysis indicates that universal opt-out ED testing would be cost-effective (assuming a willingness-to-pay [WTP] threshold of €30 000/QALY) for this profile when the HIV prevalence is 0.51% or higher.

The total life years, QALYs, costs, and cost-per-QALY for the primary and secondary analysis are present in Table 2.

Scenario analyses

The HIV prevalence threshold analysis (scenario analysis 1) demonstrated that universal opt-out ED testing is cost-effective above a prevalence of 0.25%, assuming WTP €30 000/QALY (Fig. 2). Opt-out ED testing was cost-effective for both earlier and later identification profiles (scenario analysis 2), and the value of opt-out testing was greater if SoC (the comparator) only comprised OI event IC testing (scenario analysis 3). Opt-out ED testing remained cost-effective (WTP threshold: €30 000/QALY) even when using the lower LTC parameter of 58.00% (scenario analysis 4).

See Supplementary Material S5 for complete results of scenarios 2–4.

Sensitivity analyses

The input variables with the most impact on cost-effectiveness were related to the natural history of HIV and treatment outcomes. Model predictions were generally robust to the evaluated variations, with only small changes in the ICER observed. Only the low value for the CD4 state utilities sensitivity was no longer cost-effective (Supplementary Fig. S2).

Table 2. Discounted, per-patient summary results for individuals presenting to an Italian ED with undiagnosed HIV for primary and secondary analysis

	Primary results (Vaz-Pinto profile)			Secondary results (Smout profile)		
	SoC (indicator condition)	Universal opt-out testing	Incremental	SoC (indicator condition)	Universal opt-out testing	Incremental
Life years	13.93	16.64	2.71	13.93	15.75	1.82
QALYs	10.76	13.10	2.34	10.76	12.33	1.57
Total costs	128 467€	186 315€	57 847€	128 471€	179 169€	50 698€
Cost-per-QALY	–	–	24 680€	–	–	32 220€

Abbreviations: ED: emergency department; HIV: human immunodeficiency virus; QALY: quality-adjusted life year.

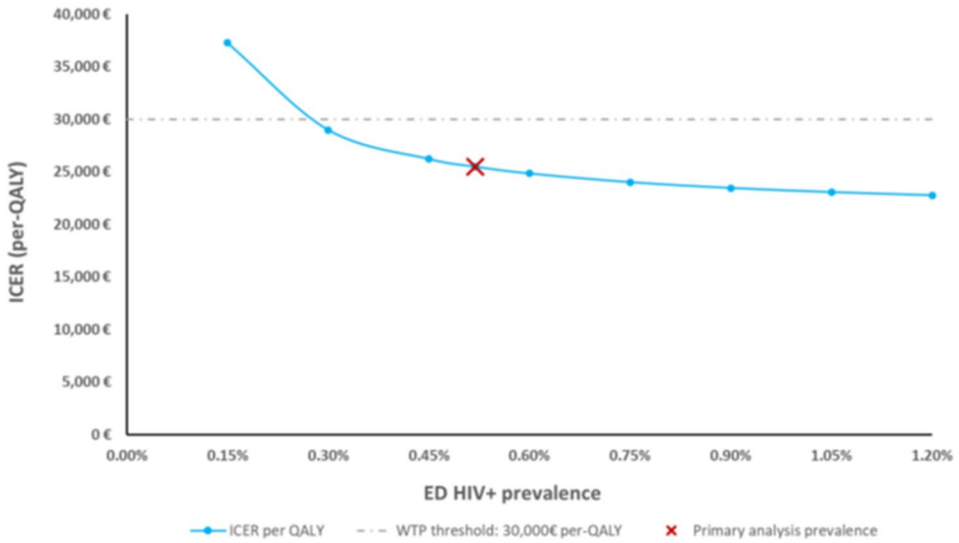

Figure 2. Incremental cost-effectiveness ratio (per-QALY) estimates for alternative ED HIV prevalence levels. Abbreviations: ED: emergency department; HIV: human immunodeficiency virus; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year.

Discussion

Main findings

The findings indicate that universal opt-out testing for HIV in Italian EDs would be cost-effective. In the primary analysis, universal opt-out ED testing resulted in 15.78 additional new diagnoses for 10 000 people presenting to the ED and was cost-effective with an ICER of €24 680/QALY. With poorer outcomes reported for late-stage presentation, early diagnosis and intervention are imperative for achieving optimal outcomes for PLWH. Universal opt-out ED testing was associated with life-year gains and higher QALYs compared to IC testing, due to an increased number of diagnoses and patients linked to care.

The secondary analysis, based on Smout *et al.*, yielded fewer additional new diagnoses (4.18 for every 10 000 people), with the ICER slightly exceeding the €30 000/QALY threshold. This discrepancy could be attributed to differences in the implementation of opt-out ED screening and the HIV prevalence in their respective populations (0.52% vs. 0.41%). A key difference in implementation was the algorithm used for automatically excluding HIV-positive individuals who had been recently tested. The English screening used a less sophisticated EPR system than Portugal's, which led to some unnecessary testing and associated costs. When assessing the potential impact of opt-out ED HIV testing in Italy, it is important to recognize that its effectiveness increases with the automation of the ordering systems used [10].

HIV prevalence is a key determinant of the cost-effectiveness of ED screening [14]. HIV prevalence in Italian EDs is largely unknown and expected to vary by and within regions (e.g. urban vs. rural areas) [4], similar to most countries. The prevalence threshold analysis demonstrated that universal opt-out ED testing is cost-effective above an HIV prevalence of 0.25% (WTP threshold of €30 000/QALY), close to the 0.2% HIV prevalence threshold in which routine ED testing is recommended in the UK by NICE [32]. This threshold can be used to guide decision-making at regional and local levels, given Italy's decentralized healthcare investment decisions.

Scenario analysis 2 indicates that universal opt-out screening would be cost-effective for both earlier and later identification profiles. The findings remained robust across other scenarios assessed.

Findings in the context of literature

A systematic review of IC testing for HIV across seven Western countries indicates that this approach leads to missed opportunities for early HIV diagnosis [33]. A recent Spanish study found that 47.8% of HIV cases were missed through this IC guided testing strategy [34]. These findings emphasize the need for alternative strategies, such as universal opt-out testing, to reduce late-stage diagnoses which result in poorer outcomes and increased healthcare costs [3, 32]. In the UK, first-year healthcare costs for late diagnosis are double compared to timely diagnosis [32].

HIV infections in older individuals remain undiagnosed for longer, leading to more advanced disease and opportunistic infection [3]. This may be because they perceive themselves as less at risk for HIV and seek testing less frequently than younger people [3, 35].

ED testing offers the benefit of reaching a broader population beyond those accessing sexual health services. In Italy, late-stage diagnoses are most common among self-reported heterosexual males over 40 [4], a group less likely to participate in current testing

approaches which are largely client-initiated and mainly target men who have sex with men [6]. Evidence from other settings suggests that implementing universal ED testing could help reduce the stigma associated with HIV testing [10, 16].

Strengths and limitations

This study is the first to estimate the potential health economic value of universal opt-out HIV testing in EDs in Italy. It provides an HIV prevalence threshold above which universal testing could be cost-effective if model assumptions are reflective of the Italian setting. The study also identifies key data gaps in Italy, which can guide future data collection and inform subsequent analyses. The findings can help prioritize areas for data collection such as local HIV prevalence, effectiveness and sustainability of best practices, stakeholder and patient opinion, and current testing rates. Due to key data gaps, some input variables were based on other European studies. Real-world data on ED HIV prevalence and ED opt-out testing outcomes in Italy would be essential for validating the model's parameters.

A scenario analysis addressed the uncertainty regarding current HIV testing rates in Italy, confirming that the intervention remains cost-effective under different SoC testing rates.

Importantly, our model likely underestimates the benefits of universal opt-out testing in Italy. Firstly, it assumes that all individuals previously diagnosed are already engaged in HIV care, thereby not accounting for the benefits of re-engaging individuals who may be disengaged [10, 16]. Secondly, the model did not capture the potential impact of reduced onward transmission which may reduce future HIV incidence, prevalence, and associated healthcare costs. Lastly, due to uncertainties in the model parameters, it only accounts for direct healthcare costs; incorporating societal costs may increase the cost-effectiveness of this strategy.

Future research and policy implications

This study highlights the potential value of universal opt-out HIV testing in EDs in Italy and can inform national discussions on optimizing testing strategies. For stakeholders to fully consider this approach, further research is needed to understand its acceptability and feasibility in Italy. The ongoing review of HIV testing consent legislation presents an opportunity for our findings to inform discussions on opt-out testing.

While this study focused on the cost-effectiveness of opt-out testing, it does not address the practical aspects of implementation within Italian EDs. We also acknowledge that increased testing will require novel linkage to care pathways to manage an increased number of diagnoses. Considering the current resources and infrastructure, further research should explore the necessary changes for successful integration of this screening into clinical practice. Moreover, a real-world implementation study of opt-out testing is needed to determine opt-out testing outcomes in Italy and re-assess its cost-effectiveness as new data becomes available. Additionally, both combined opt-out screening and linkage to care and modelling the cost-effectiveness of simultaneous screening for multiple BBVs such as HIV, hepatitis B and C should be a public health priority. BBV screening in the ED setting has successfully been implemented in other European countries [13, 36] and may increase cost-effectiveness compared HIV opt-out testing alone [37–39].

Conclusions

Universal opt-out ED testing could be a cost-effective strategy to increase the number of new HIV diagnoses and improve HIV health outcomes in Italy. The full benefit is likely underestimated as the model did not consider averted transmissions or re-engagement in the care of people previously diagnosed with HIV. Further real-world epidemiologic and implementation research is needed to verify the findings.

Acknowledgements

We express our gratitude to Alex van Doornewaard for his input in conceptualizing and developing the model and his thoughtful contribution to the interpretation of the results. We also thank Roberto Caldera and Leonardo Martello for their support in identifying and liaising with Italian clinical experts and assisting in sourcing Italian HIV treatment market share data. We acknowledge Dr Barbara Suligoi (Director of National AIDS Unit, Istituto Superiore di Sanita) for confirming that systematic collection of data on HIV testing rates and regional HIV prevalence is currently lacking in Italy.

Author contributions

Enyal Lani and Eva Kagenaar worked on the model conceptualization, model parameterization, scenario analyses and interpretation of results. Eva Kagenaar also contributed to model built. James Jarrett and Murad Ruf contributed to the study design and results interpretation. Antonella d'Arminio Monforte, Gabriella d'Ettorre, Gioacchino Galardo, and Walter Ricciardi validated the model structure and input parameters and contributed to scenario analysis design and results interpretation. Susie Huntington contributed to the interpretation of the results. Enyal Lani led on the drafting and editing of the article with input and support from Susie Huntington. Antonella d'Arminio Monforte, Eva Kagenaar, Murad Ruf, and James Jarrett and contributed to the article development. All authors reviewed and approved the final article.

Supplementary data

Supplementary data are available at *EURPUB* online.

Conflict of interest: At the time of writing, E.L., E.K., and S.H. were employed by Aquarius Population Health which received funding for this study. Aquarius Population Health is an independent consultancy working on projects related to diagnostics for different commercial and academic clients and as part of grant-funded projects. M.R. and J.J. are employees of Gilead Sciences, whose portfolio includes HIV therapeutics. A.d.A.M., G.d.E., G.G., and W.R. have received honoraria from Gilead Sciences for their participation in the clinical expert panel of this project. A.d.A.M. has also received institutional grants from Gilead, ViiV, and MSD, both from their Italian and international branches. G.d.E. has also received grants from Gilead, ViiV, MSD, and Janssen, and honoraria for lectures, presentations from Gilead, ViiV, MSD, Janssen, AbbVie, and Pfizer.

Funding

This study was funded by Gilead Sciences.

Data availability

All data relevant to the study are included in the article or uploaded as supplementary material. The model is not publicly available.

Public and patient involvement

No patients were involved in the design, conduct, reporting, or dissemination plans of this research.

Ethics approval

No ethical approval was required or sought as only secondary data sources were used, there was no randomization or change to patient care, and no patient-identifying information was obtained or used.

Key points

- Exceptionally high proportion of late-stage HIV diagnoses (~10% higher than the European average) remains a critical challenge in Italy, contributing to higher morbidity, mortality, and healthcare costs.
- This study suggests that universal opt-out HIV testing in Italian EDs could be a cost-effective strategy to increase new HIV diagnoses and improve health outcomes.
- Our health economic model may underestimate the full benefits of this intervention as it does not consider transmissions averted or the re-engagement of individuals previously diagnosed with HIV but not in care.
- Our findings could inform regional and national discussions on adopting novel HIV testing strategies in Italy.
- Further Italian epidemiological and real-world implementation data are needed to validate these findings and guide policy decisions.

References

1 Trickey A, Zhang L, Sabin CA, Sterne JAC. Life expectancy of people with HIV on long-term antiretroviral therapy in Europe and North America: a cohort study. *Lancet Healthy Longev* 2022;**3**:S2.

2 Waters L, Sabin CA. Late HIV presentation: epidemiology, clinical implications and management. *Expert Rev Anti Infect Ther* 2011;**9**:877–89.

3 Popping S, Versteegh L, Nichols BE *et al.*, ATHENA observational cohort. Characteristics and short- and long-term direct medical costs among adults with timely and delayed presentation for HIV care in The Netherlands. *Plos One* 2023; **18**:e0280877.

4 L'Istituto Superiore di Sanità. Notizario dell'Instituto Superiore di Sanita—Aggiornamento delle nuove diagnosi di infezione da hiv e dei casi di aids in Italia. 2023. https://www.salute.gov.it/imgs/C_17_pubblicazioni_3377_allegato.pdf

5 Ministerio della Salute. Conferenza di Consenso sul Test HIV: Quesiti e risposte. Italy. https://www.salute.gov.it/imgs/C_17_notizie_1265_listaFile_itemName_6_file.pdf. Date accessed 1 May 2024.

6 Galli M, Borderi M, Viale P. HIV policy in Italy and recommendations across the HIV care continuum. *Infez Med* 2020;**28**:17–28.

7 Ministero della Salute. Documento di consenso sulle politiche di offerta e le modalità di esecuzione del test per HIV in Italia. https://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp? id=1647. Date accessed 28 June 2023.

8 Barbanotti D, Tincati C, Tavelli A *et al.* HIV-indicator condition guided testing in a hospital setting. *Life Basel Switz* 2023;**13**:1014. https://doi.org/10.3390/life13041014

9 UNAIDS. AIDS targets. 2025. https://www.unaids.org/sites/default/files/2025-AIDS-Targets_en.pdf. Date accessed 3 July 2024.

10 Simmons R, Plunkett J, Cieply L *et al.* Blood-borne virus testing in emergency departments—a systematic review of seroprevalence, feasibility, acceptability and linkage to care. *HIV Med* 2023;**24**:6.

11 European Centre for Disease Prevention and Control. ECDC Guidance: HIV testing: increasing uptake and effectiveness in the European Union. 2010. https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/101129_GUI_HIV_testing.pdf. Date accessed 1 May 2024.

12 European Centre for Disease Prevention and Control/WHO, Regional Office for Europe. HIV/AIDS surveillance in Europe 2021–2020 data. Stockholm: ECDC, 2021. https://www.ecdc.europa.eu/sites/default/files/documents/2021-Annual_HIV_Report_0.pdf. Date accessed 1 May 2024.

13 Department of Health and Social Care, NHS England. New research into expansion of life-saving HIV testing programme. https://www.gov.uk/government/news/new-research-into-expansion-of-life-saving-hiv-testing-programme. Date accessed 28 March 2024.

14 Mwachofi A, Fadul NA, Dortche C *et al.* Cost-effectiveness of HIV screening in emergency departments: a systematic review. *AIDS Care* 2021;**33**:1243–54.

15 Parry S, Bundle N, Ullah S *et al.* Implementing routine blood-borne virus testing for HCV, HBV and HIV at a London Emergency Department—uncovering the iceberg? *Epidemiol Infect* 2018;**146**:1026–35.

16 Smout E, Phyu K, Hughes GJ *et al.* Real-world clinical effectiveness and sustainability of universal bloodborne virus testing in an urban emergency department in the UK. *Sci Rep* 2022;**12**:19257.

17 Vaz-Pinto I, Gorgulho A, Esteves C *et al.* Increasing HIV early diagnosis by implementing an automated screening strategy in emergency departments. *HIV Med* 2022;**23**:1153–62.

18 Hill-Trout R. *Implementation of Routine Opt out Blood Borne Virus (BBV) Screening in 34 Emergency Departments (EDs) in Areas of Extremely High HIV Prevalence in England*. Gateshead, UK: NHSE BHIVA.

19 Parker B, Ward T, Hayward O, *et al.* Cost-effectiveness of the long-acting regimen cabotegravir plus rilpivirine for the treatment of HIV-1 and its potential impact on adherence and viral transmission: a modelling study. *PloS One* 2021; **16**:e0245955.

20 Butler K, Anderson S-J, Hayward O *et al.* Cost-effectiveness and budget impact of dolutegravir/lamivudine for treatment of human immunodeficiency virus (HIV-1) infection in the United States. *J Manag Care Spec Pharm* 2021;**27**:891–903.

21 EACS Guidelines Version 11.1. EACS, 2022. https://www.eacsociety.org/media/guidelines-11.1_final_09-10.pdf.

22 Agenzia Italiana Del Farmaco. Linee guida per la compilazione del dossier a supporto della domanda di rimborsabilità e prezzo di un medicinale. 2019.

23 Husereau D, Drummond M, Augustovski F *et al.*, CHEERS 2022 ISPOR Good Research Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *BMJ* 2022;**376**:e067975.

24 Perry KR, Ramskill S, Eglin RP *et al.* Improvement in the performance of HIV screening kits. *Transfus Med* 2008;**18**:228–40.

25 d'Arminio Monforte A, Sabin CA, Phillips A *et al.*, Antiretroviral Therapy Cohort Collaboration. The changing incidence of AIDS events in patients receiving highly active antiretroviral therapy. *Arch Intern Med* 2005;**165**:416–23.

26 Regionale Lombardia. Lombardia Nomenclatore Tariffario Regionale 2022. 2022.

27 National Institute for Health and Care Excellence. Overview | Cabotegravir with rilpivirine for treating HIV-1 | Guidance | NICE. 2022. https://www.nice.org.uk/guidance/ta757. Date accessed 18 December 2023.

28 Alcantarini C, Bargiacchi O, Farenga M *et al.* HIV E AIDS in piemonte. 2022. https://www.seremi.it/sites/default/files/Report%20HIV%202019%20-%202021%20%20%28ed.%202022%29.pdf.

29 IstatData—Prices—Consumer Prices for the whole nation. I.Stat. http://dati.istat.it/?lang=en. Date accessed 2 August 2023.

30 Restelli U, Rizzardini G, Antinori A *et al.* Cost-effectiveness analysis of dolutegravir plus backbone compared with raltegravir plus backbone, darunavir + ritonavir plus backbone and efavirenz/tenofovir/emtricitabine in treatment naïve and experienced HIV-positive patients. *Ther Clin Risk Manag* 2017;**13**:787–97.

31 Regione Lombardia Direzione Generale Welfare. Percorso diagnostico therapeutico assistenziale (PDTA) del paziente affetto da infezione/malattia HIV/AIDS anno 2021. 2021. https://www.simit.org/images/regioni/lombardia/comunicazioni/Documenti%20Regionali/PDTA%20HIV%20Regione%20Lombardia%202021.pdf. Date accessed 17 November 2023.

32 National Institute for Health and Care Excellence. HIV testing: increasing uptake among people who may have undiagnosed HIV. 2016. https://www.nice.org.uk/guidance/ng60/history. Date accessed 7 May 2024.

33 Bogers SJ, Hulstein SH, Schim van der Loeff MF *et al.*, HIV Transmission Elimination AMsterdam (H-TEAM) Consortium. Current evidence on the adoption of indicator condition guided testing for HIV in Western countries: a systematic review and meta-analysis. *eClinicalMedicine* 2021;**35**:100877.

34 Ortega E, Ocete MD, Martínez-Roma M *et al.* Reassessing HIV detection strategies: an analysis of opportunistic screening vs. indicator-condition-driven diagnosis in Valencia, Spain. *J Community Health* 2024;**49**:748–54. https://doi.org/10.1007/s10900-024-01326-9

35 Centers for Disease Control and Prevention. HIV declines among young people and drives overall decrease in new HIV infections. https://www.cdc.gov/media/releases/2023/p0523-hiv-declines-among-young-people.html. Date accessed 15 May 2024.

36 UK Health Security Agency. Emergency department bloodborne virus opt-out testing: 12-month interim report 2023. 2023. https://www.gov.uk/government/pub

lications/bloodborne-viruses-opt-out-testing-in-emergency-departments/emergency-department-bloodborne-virus-opt-out-testing-12-month-interim-report-2023#main-messages. Date accessed 15 May 2024.

37 Falla AM, Hofstraat SHI, Duffell E *et al.* Hepatitis B/C in the countries of the EU/EEA: a systematic review of the prevalence among at-risk groups. *BMC Infect Dis* 2018;**18**:79.

38 Stroffolini T, Stroffolini G. Five decades of HBV infection in Italy: a continuous challenge. *Biology* 2023;**12**:1075.

39 Williams J, Vickerman P, Douthwaite S *et al.* An economic evaluation of the cost-effectiveness of opt-out hepatitis B and hepatitis C testing in an emergency department setting in the United Kingdom. *Value Health* 2020;**23**:1003–11.

European Journal of Public Health, 2025, 00, 1–8
https://doi.org/10.1093/eurpub/ckaf057
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