The Role of Targeted HIV Screening in the Emergency Department

THE ROLE OF TARGETED HIV SCREENING IN THE EMERGENCY DEPARTMENT: A SCOPING REVIEW

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ABSTRACT

Background. Human immunodeficiency virus (HIV) infection continues to expand worldwide and a significant proportion of infection is still undiagnosed. Recent studies have addressed the impact and feasibility of *'opt-out'* HIV screening in Emergency Departments (EDs) in urban settings at high HIV prevalence, whereas little is known about the yield of implementing *'targeted'* HIV testing especially in low-prevalence areas.

Objective. The present study undertakes a scoping review of research carried out on the implementation of targeted HIV screening in adult EDs to determine the impact, feasibility and acceptability of HIV testing in different HIV prevalence settings.

Design. Online databases (EMBASE, MEDLINE) were used to identify papers published between 2000 to 2020. A three-concept search was employed with HIV (HIV, Human immunodeficiency virus infection, HIV infections), targeted testing (Target, screening or testing) and emergency medicine (Emergency Service, emergency ward, A&E, accident and emergency or Emergency Department) (28th February 2020). Only full-text articles written in English, French, Spanish or Italian and using impact and/or feasibility and/or acceptability of the program as primary or secondary outcomes were analysed.

Results. The search returned 416 articles. Of these, 12 met inclusion criteria and were included in the final review. Most of the included studies were carried out in the United States (*n*=8; 67%) and in areas of high HIV prevalence (*n*=11; 92%). Three (20%) were randomized control studies. While the rate of newly diagnosed HIV cases varied widely (0.03-2.2%), likely due to methodological heterogeneity between studies, the linkage of new HIV diagnosis was often high (80-100%) and median CD4+ cell count was always greater than 200 cells per microliter. Targeted HIV screening was found to be cost-effective (out of 2 studies) and well accepted by participants (out 2 studies).

Conclusions. Targeted HIV screening at the ED can be impactful, feasible and well accepted, but often requires extra funding and staff. Most previous work has focused on areas of high disease prevalence.

INTRODUCTION

Considerable steps forward have been achieved in terms of Human Immunodeficiency Virus (HIV) knowledge and antiretroviral therapy (ART) over the last 30 years. Despite this, the overall number of People Living with HIV (PLHIV) is still rising [1]. All the more alarming, is the statistic from the European Centre for Disease Prevention and Control (ECDC) 2017 report that up to one quarter of PLHIV are unaware of their HIV status [2].

As part of the international effort to globally counteract the Acquired Immune Deficiency Syndrome (AIDS) epidemic, the United Nations HIV/AIDS (UNAIDS) Program has set the ambitious *90-90-90 targets* by 2020: 90% of all people with HIV diagnosed, 90% of those diagnosed to be on antiretroviral treatment, and 90% of those on treatment being virally suppressed [3]. Wider access to HIV testing remains therefore a challenge to urgently overcome.

Delayed HIV diagnosis increases the risk of severe complications and premature mortality [4,5,6,7,8,9,10,11], as well as the chance of virus transmission [12,13,14], ultimately leading to major resource usage and healthcare cost [15,16,17,18,19,20]. Therefore, a systematic HIV screening program could be of benefit not only to the patient but also to the whole community.

HIV testing is becoming increasingly prevalent as part of routine in-hospital investigations for certain group of patients, such as those electively undergoing surgery or pregnant women during prenatal care [21,22,23,24,25,26,27,28,29,30,31,32]. However, those interventions selectively target only a limited group of patients that have access to specific health care facilities.

It is well accepted that the ED can offer a strategic point of testing for a number of healthcare conditions [33,34,35,36,37,38,39,40,41,42,43,44,45]. In the UK, similar to many European countries, almost a quarter of the country's population attend an ED every year making it a sensible place to introduce an HIV testing program [46,47]. Moreover, the ED offers 24/7 assistance to marginalized and traditionally underserved populations (e.g. migrant people, homeless, intravenous drugs users) in whom HIV is known to be more prevalent [48,49,50,51,52].

Two main approaches to delivery of screening are suggested by HIV testing guidelines: (1) a universal screening strategy aiming to test people aged 13 to 64 years in all clinical settings unless the patient declines ("*opt-out"* screening), or (2) a targeted strategy in which the test is offered to individuals presenting with indicator conditions [53,54,55] Although the universal "*opt-out"* screening is by far the best strategy to detect HIV early in the asymptomatic stage of the infection,

it has been shown to be cost-effective only in populations with an HIV prevalence greater than 0.1% [56].

In light of recommendations issued by national and international agencies (*Centre of Disease Control and Prevention*; CDC, the ECDC, the *British HIV association*; BHIVA and the *National Institute for Health and Care Excellence*; NICE), routine non-targeted HIV screening has been adopted in some EDs located in areas of high-HIV prevalence [2,57,58,59]. However, currently EDs are overstretched and the dedicated funding to support universal testing is not widely available. On the other hand, no clear recommendation has been issued so far regarding targeted HIV screening and evidence about its ED implementation is sparse. Identifying the most effective approaches to screening will allow better implementation and more evidence of the yield of screening in areas at lower HIV prevalence is still required.

The main objective of this scoping review is to investigate the impact, feasibility and acceptability of a systematic targeted HIV testing program at the ED, especially in areas at low HIV prevalence.

METHODS

The final protocol was registered on Open Science Framework on 6th February 2020 (https://osf.io/ajyec/) and is available on request from the corresponding author.

To be included in the review, papers needed to focus on targeted HIV screening in the ED. A three-concept search including HIV (HIV, Human immunodeficiency virus infection, HIV infections), targeted testing (Target, screening or testing) and emergency medicine (Emergency Service, emergency ward, A&E, accident and emergency or Emergency Department) was initially run without any restrictions and two (O.S., B.G. – 28th February 2020) authors screened each result.

Peer-reviewed journal papers were included if they were:

- published between 2000-2020
- written in English, French, Spain or Italian
- full-text articles
- ED-centered, or where ED data could be extracted

- involving adults (aged > 16 years)
- including outcomes of impact and/or feasibility and/or acceptability [Table 1]

Papers were excluded if they were:

- centered on "non-targeted" or *"opt-out"* HIV screening strategy
- limited to specific setting (e.g.. veterans)
- descriptive case series, survey, review, study protocol, serosurvey, comparison among laboratory techniques

In order to identify potentially relevant documents, the bibliographic databases MEDLINE and EMBASE were searched from 2000-2020. Grey literature was hand-searched through Google Scholar, conference proceedings, ClinicalTrial.gov and OpenGrey for unpublished research.
The search strategies were drafted by an experienced librarian [M.D.] and further refined through team discussion. The final search strategy for MEDLINE and EMBASE can be found in Appendix 1.
The final search results were exported into EndNote, and duplicates were removed by a library technician.

Two reviewers independently evaluated the titles, abstracts and then full text of all publications identified by our initial search for potentially relevant publications. We resolved disagreements on study selection and data extraction by consensus and discussion with other reviewers if needed.

A data-charting form was jointly developed by two reviewers to determine which variable to extract [Table 2]. The two reviewers independently charted the data, discussed the results and continuously updated the data-charting form in an iterative process.
Data from eligible studies were charted using a standardized data extraction tool designed for this study. The tool captured the relevant information on key study characteristics and detailed information on all metrics used to estimate previously listed outcomes anywhere in the article. Any disagreements were resolved through discussion between the two reviewers or further adjudication by a third party if necessary.
We abstracted data on article characteristics (country of origin, study population and sample size), methodology/methods (study design, type of test, funding/staff model, aims/purpose, outcome measure) and key results.

We grouped the studies by predefined outcomes investigated (impact, feasibility and acceptability) [Table 1] and summarized the study designs for each group, along with the measures used and broad findings [Table 2].

High HIV prevalence was defined as local authorities with a diagnosed HIV prevalence of between 2 and 5 per 1000 people aged 15 to 59 years (NICE 2016). High patient volume ED was defined as receiving over 50,000 patients annually or covering an urban area of more than 600,000 inhabitants. Study funding was classified as government funding, commercial funding and non-profit foundations (e.g. charities).

RESULTS

After duplicates were removed, a total of 241 citations were identified from searches of electronic databases and review article references. Based on the title and the abstract, 167 were excluded, with 44 full-text articles to be retrieved and assessed for eligibility. Of these, 32 were excluded for the following reasons:

- Study design did not fit with eligibility criteria (*n*=9)
- Only abstract for conference (*n*=16)
- Review – data already extrapolated (*n*=2)
- Review – data could not be extrapolated (*n*=2)
- Limited to specific setting (*n*=2)
- Out of study search study time span (*n*=1)

The remaining 12 studies were considerate eligible for this review [Figure 1]. The list of excluded papers with reason can be found in Appendix 2.

Studies' characteristics, methodology and key results are presented in Table 2.

All papers were published between 2005 and 2019. Most of the included studies were carried out in the Unites States (*n*=8; 67%)[60,61,63,64,65,66,67] and in area at high HIV prevalence (2 and 5

per 1000 people tested; > 0.20%) (*n*=11; 92%) [60,61,62,64,65,66,67,68,69]. 6 studies were performed in EDs receiving a high volume of patients (defined as over 50,000 patients annually or covering urban area of more than 600,000 inhabitants) [62,63,64,66,69].

The study period varied from 4 months to 6 years.

In terms of study design, 25% (*n*=3) included studies that were randomized controlled trials (RCT) [62,64,68]. Of these, one was a randomized cross-over design study, one a cluster-randomized trial (CRT) comparing targeted vs non-targeted HIV screening and one a 2-period cluster-randomized crossover trial (CRXO) comparing targeted HIV screening vs diagnostic testing. 3 (25%) were prospective studies: two evaluating targeted HIV screening vs diagnostic testing and one comparing targeted HIV screening to non-targeted HIV screening [60,66]. The remaining papers included were retrospective studies (*n*=4; 33%) [61,63,65], a cost-utility study (*n*=1) [67] and a post-analysis study (*n*=1) [69].

Two different methods of HIV testing were adopted: rapid bedside HIV assessment (*n*=8; 67%), conventional ELISA with confirmatory Western blot (*n*=3; 25%) or both (*n*=1; 8%).

Although all studies were government funded, two were also supported by commercial funding. In 5 studies (42%) the HIV screening was entirely run by ED staff including physicians, nurses, nurse practitioners and social workers.

The majority of studies (*n*=8; 67%) primarily focused on measures of impact of targeted HIV screening, whereas one entirely addressed patient acceptability and one was centered on program feasibility. Of the two remaining studies, one equally included measures of impact and feasibility while the other was focused on both impact and acceptability.

The main findings of the studies are discussed below.

Impact

The rate of newly diagnosed HIV cases was the most investigated measure of impact among included studies. This figure varied widely from 0.03 to 2.2%, mainly due to heterogeneity in methodology and definitions. In the two studies reporting the highest rate of new HIV diagnoses, the number of new diagnoses was compared to the number of patients tested and not to the total population included [60,61]. In both studies the number of patients refusing the test was not reported. In contrast, the study with the lowest rate of newly diagnosed HIV cases (0.03%) was a 2-

period CRXO carried out in France where the number of new HIV diagnoses was compared to a denominator made up all patients approached [62]. Comparing the number of new HIV diagnoses to a denominator made up only of patients who were tested led to an increase in the prevalence of newly diagnosed HIV cases to 0.7%. In the only study carried out in a low prevalence area (0.16%), the rate of new HIV diagnoses was 0.7%, therefore still comparable to the above study performed in a high prevalence setting [63]. The rate of new HIV diagnosis, defined as new cases divided by patients tested, was greater in low compared with high volume EDs (low volume ED: 1.2, 1.4, 2.2, 2.2 vs high volume ED: 0.7, 0.22, 0.7, 1.3).

Another measure of impact taken into account by many studies was the linkage to care, defined as the proportion of patients with new HIV diagnosis attending follow-up care at the infectious disease center. This value was often high, between 80 and 100%. The only exception was the targeted arm of the CRT carried out in US by Lyons MS et al (2013) where only two of three new HIV diagnosis were successfully linked to care [64].

CD4+ cell count was reported in only two studies focused on impact of targeted HIV screening. In the retrospective study led by Christopoulos KA (United States 2011) the median CD4+ cell count at diagnosis was 268 cells per microliter [65]. During the targeted period of the prospective study carried out by Haukoos JS (United States 2013) the median CD4+ cell count was 244 cells per microliter (vs 272 during the non-targeted period) [66].

Feasibility

Two studies addressed economic analysis of targeted HIV screening. Dowdy DW et al. performed a cost-utility analysis of a screening program entirely supported by ED staff over 4 months in an urban ED in San Francisco (United States 2011): largely because of its benefit in preventing HIV transmission, for every patient tested, targeted screening was shown to save 112 US Dollars [67]. In contrast, according to the results of the CRXO carried out by Leblanc J et al. in multiple EDs in Paris (DICI-VIH study - France 2018), the incremental cost per additional new diagnosis was 1324 Euros [62].

Acceptability

Two European studies were focused on patient acceptability of HIV targeted screening in the ED. In the RCT performed by Gillet C. et al (Switzerland 2018), patient acceptance in the targeted arm was 48% and was not significantly different when compared to the non-targeted arm [68]. In a post-analysis of the DICI-VIH study, Leblanc J. et al. showed how patient acceptance varied from 64 to 77% across EDs, increasing with research staff involvement and decreasing over time (France 2019) [69].

DISCUSSION

Our scoping review shows that targeted HIV screening at the ED has proved to be impactful, feasible and well accepted in the ED population, but may require increased staffing resource and extra funding. Despite being tested in high-HIV prevalence setting in most of the cases, targeted screening might be appropriate also in low prevalence areas.

Although the majority of studies in this scoping review were from the US between 2005 and 2013, those based in Europe (France, Spain and Switzerland) were more recent (2018-2019).
Study design varied between prospective and retrospective studies, with one third of evidence arising from RCTs. Despite most of the studies included addressing measures of impact, the rate of new HIV diagnosis was not easily comparable given methodological variability. In this regard, retrospective studies may over-estimate this outcome normalizing new HIV diagnosis to the number of patients tested, and not to the total approached. Interestingly, the only study carried out in a low HIV prevalence area reported a rate of new HIV diagnosis still comparable to other studies performed in a high prevalence setting [63]. The volume of patients may also play a role on measures of impact with low volume EDs showing a higher rate of new HIV diagnosis. This can be easily explained by the evidence that when ED becomes overstretched, especially in a staff-limited setting, clinical activities take over research/screening projects [70,71,72,73].

The high burden of HIV infection worldwide and the large proportion of PLHIV unaware of their serostatus means that early HIV detection represents a crucial public health challenge [1,74,75]. This is especially true given ART availability, its effectiveness in reducing viral load and its beneficial

effects in term of survival rate and morbidity particularly at this stage of the infection [76,77]. Moreover, it is well recognized that early HIV identification may have a role in prevention of virus transmission from index cases to uninfected people [76,77,78,79]. HIV screening is therefore key not only for successful treatment but also for infection prevention. Therefore, many international and national agencies (CDC, BHIVA, the NICE and ECDC) have been supporting the deployment of effective public health measures in this regard. Although HIV testing has been traditionally offered in limited health care settings (e.g. Sexual Health clinics) [80,81], it has been expanded in non-traditional settings in the attempt to make it more accessible, ED being one of these areas. Indeed, it is well recognised that the ED might play a crucial role in HIV screening since it treats patients who may not normally use the health system and may be at increased risk of infection [48]. Moreover, routine blood samples are likely to be part of ED clinical care and can be easily used for testing [82].

On the grounds of these considerations, "*opt-out"* HIV screening at the ED was firstly introduced in the US as part of routine medical care for all patients aged 13-64 years in areas with HIV prevalence greater than 0.1% (CDC 2006) [57]. However, evidence of success and long-term sustainability were debatable. Similarly, despite the endorsement of the ECDC for universal screening in settings at high HIV prevalence (2017), the situation across Europe is quite diverse [2]. In the UK, BHIVA (2008) and NICE (2016) published guidelines for HIV testing in all patients attending the ED in high (2-5/1000) and very high (5 or over/1000) risk areas [58,59]. London was the first city in the UK to offer non-targeted HIV screening in the ED, given that the overall prevalence of HIV in London is 5.4/1000 (England 1.9/1000) [83]. Reports of these experiences showed that non-targeted testing was feasible and well accepted by staff and patients and did not adversely affect length of ED stay when offered to patients having routine blood tests [84,85,86,87,88,89,90,91,92]. However, non-targeted screening requires many tests and may include patients previously known to have a HIV positive status. Concerns therefore persist about its feasibility and effectiveness in the long run especially in setting at lower HIV prevalence [93,94,95,96,97,98]. On the other hand, testing selectively increases the likelihood of new HIV diagnoses whilst running fewer tests, but requires actively selecting patients to be offered the test increasing the workload and thought process for busy ED staff.

The results of our scoping review show that the interest in targeted HIV screening at the ED is now moving from the US to Europe, with the latest studies being carried out in France, Spain and Switzerland. Although there is a growing body of evidence around the implementation of targeted HIV screening in European EDs, there is no published UK experience, thus far.

The gap between national recommendations and ED test implementation in the real-world points towards two main challenges to overcome: The need for extra staff and for supplementary funding (equipment, laboratory services etc).

Despite studies comparing targeted vs non-targeted testing showing that targeted testing may lead to fewer tests being performed, and hence being cheaper on the number of assays being performed, additional testing (rather than blanket non-targeted testing) in the ED requires extra staff time [64,68]. Schrantz SJ (2011) and Leblanc J (2019) found that testing frequency decreased over time after introduction when screening was carried out by ED staff [61,69]. Moreover, the post hoc analysis of the DICI-VIH study shows that questionnaire distribution was higher on weekdays and when research staff were available but decreased over time and when demand on the ED increased [69]. This is in line with the results of our scoping review where low volume EDs showed a higher rate of new HIV diagnosis. Therefore if this is to be introduced outside the scope of a well-resourced research study, thought is required as to how this extra workload on staff would be managed, and who would be best placed to perform it to keep the screening program running effectively in the long run and to sustain good practice. The key aspect of screening is patient selection and questionnaire distribution which is problematic in an environment such as the ED. On the other hand, it was found that this role might be able to be fulfilled also by well-trained non-health workers. For example, in the RCT carried out by Gillet, C et al., patient selection and questionnaire distribution was entirely conducted by an appropriately trained medical student [68].

The results of our scoping review should be interpreted in light of several limitations. First of all, only one study was found that was carried out in a low HIV prevalence setting, therefore our findings may not be generalizable in areas of lower prevalence.
Secondly, it should be considered that given differences in health care systems, data from the US might not be comparable to Europe and that different targeted HIV screening protocols may differ in selection criteria.

Finally, all of our included studies were performed as part of well-resourced research studies. There may be many EDs across Europe and the rest of the world that have implemented HIV testing (either targeted or non-targeted) and have not reported the findings of their practice.

CONCLUSIONS

Targeted HIV screening at the ED can be impactful, feasible and well accepted among ED encounters, but its long-term implementation requires extra funding and supplemental staff limiting its application in low resources setting.
More studies carried out in areas of low HIV prevalence are warranted. Moreover, more data coming from low and middle-income countries are needed.

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Table and Figure legends:

Figure 1: Study flow chart

Table 1: Predefined outcomes of impact, feasibility and acceptability

Table 2: Summary of articles

Figure 1: Selection of included studies

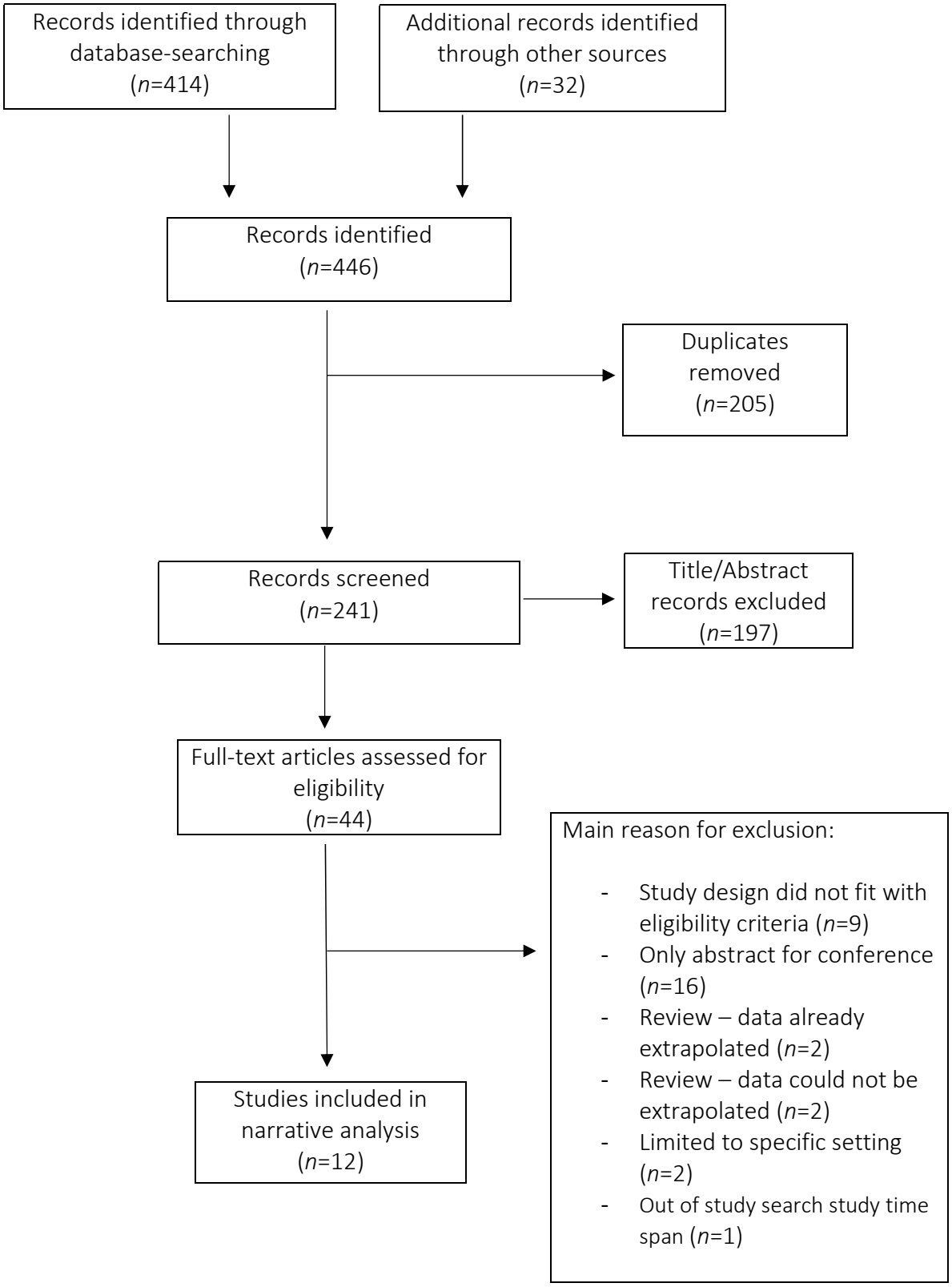

Table 1

IMPACT	Rate of new HIV cases Rate of “early” HIV diagnosis Linkage to care of patients with newly Diagnosed HIV
FEASIBILITY	Staff compliance Cost/efficacy overview
ACCEPTABILITY	Patient test acceptance

Table 2

Author(s), (*journal* and year of publication)	Country of origin, [HIV-prevalence][§]	Sample size, [study period]	Study design	Type of test(s)	Funding, Staffing model	Aims/Purpose	Outcome measures	Key findings
Gillet, C. (*PLoS ONE* 2018) [68]	Switzerland, [0.20-0.50%], Low volume ED°	*n*=160 [4-month]	RCT* (targeted vs non-targeted HIV test)	Rapid	Government funding, Supplemental staff^	1. Test the use of electronic tablets to offer testing 2. Examine whether non-targeted screening increased testing rate	HIV testing rate	a. Testing rate was lower in targeted vs non-targeted arm (10 vs 48%) b. Acceptance rate did not differ between targeted vs non-targeted arm (48 vs 53%)
Leblanc, J. DICI-VIH study (*Ann Emerg Med* 2018) [62]	France, [0.20-0.50%], High volume ED°°°	*n*=148.327 [1-year]	2-period CRXO** (targeted test vs control strategy) Multi-centers	Rapid	Government/Commercial funding, Supplemental staff^	1. Compare effectiveness of nurse-driven targeted HIV screening to standard practice 2. Compare cost-effectiveness of the two strategies	1. Proportion of new HIV diagnosis 2. Intervention's incremental cost per additional diagnosis	a. Proportion of new HIV diagnosis was higher in targeted test vs standard practice (3.0/10.000 vs 0.8/10.000) (0.03%) (0.7%) b. The incremental cost was 1.324 EU per additional new diagnosis
Leblanc, J. DICI-VIH study (*Worldviews Evid Based Nurs* 2019) [69]	France, [0.20-0.50%], High volume ED°°°	*n*=148.327 [1-year]	Post-analysis	Rapid	Government/Commercial funding, Supplemental staff^	Investigate factors associated with the implementation of targeted HIV screening	1. Proportion of questionnaires distributed 2. Proportion of testes accepted	a. Questionnaire distribution proportions were higher on weekdays and when research staff participated. They decreased over time and with increased ED volume. b. Patient acceptance increased with research staff participation and decreased over time.

Gomez-Ayerbe, C. DRIVE study (*PLoS One* 2019) [99]	Spain, [0.35%][§§], Low volume ED°	*n*=1631 [3-year]	Prospective evaluation study (targeted HIV test vs standard practice)	Rapid	Government funding, Supplemental staff	Evaluate the impact of targeted HIV screening program in comparison to standard practice	1. n° of newly diagnosed HIV patients 2. Testing coverage	Rate of newly diagnosed HIV patients and testing coverage was significantly higher in the targeted HIV testing program than in clinical practice (14/1000 vs 6/1000) (1.4%)
Lyons, M. S. (*J Acquir Immune Defic Syndr* 2013) [64]	United States, [0.36%][§§], High volume ED°°	*n*=9.572 [2-year]	CRT*** (targeted vs non-targeted HIV test)	ELISA, Rapid	Government/Commercial funding, Supplemental staff	Compare n° of new HIV diagnosis among the two strategies	1. Proportion of new HIV diagnosis 2. Proportion of eligible/approachable patients tested; acceptance rate; risk profile of tested patients; notification rate; n° of newly diagnosed patients linked to care; reasons for declining testing; initial CD4 count in newly diagnosed patients	a. Proportion of new HIV diagnosis was only slightly lower in targeted vs non-targeted arm (0.22% vs 0.31%) b. Testing rate was remarkably higher in non-targeted vs targeted arm (40.7% vs 29.7%) c. Targeted arm: 66% linkage to care
Dowdy, D. W. (*Acad Emerg Med* 2011) [67]	United States, [0.20-0.50%], Low-volume ED°	*n*=3.766 [4-month]	Cost-utility analysis	Rapid	Government funding, ED staff	Evaluate cost-effectiveness of a previously implemented targeted HIV screening program	1. Cost of the program 2. n° of QALYs**** gained; n° of estimated HIV transmission events prevented	a. Per patient tested, targeted screening saved 112 Dollars and resulted in 2.71 QALYs gained b. Targeted test prevented an estimated 2.1 HIV transmission events over 16 months
Hudepohl, N. J. (*Ann Emerg Med* 2011) [100]	United States, [0.20%], High volume ED°°	*n*=11.503 [6-year]	Retrospective observational study	ELISA	Government funding, Supplemental staff	Evaluate the cumulative effect over time of a previously implemented	1. Proportion of patients tested who reported a previous test/had a previous test within the program	Targeted HIV testing program can have relevant cumulative effects over time since a sizeable proportion of patients returns to the ED more

						targeted screening program	2. The cumulative proportion of patients tested in the program	than once (2.6% visits provided with test; 6.9% patients tested)
Haukoos, J. S. (*Acad Emerg Med* 2007) [60]	United States, [0.20-0.50%], Low volume ED°	*n*=681 [30-month]	Prospective cohort study	Rapid	Government funding, ED staff	Test a physician-based targeted HIV model	1. Characterize patients identified by the model 2. Proportion of patients completing counseling, testing and referral 3. n° of newly diagnosed HIV patients and proportion of these linked to care	Only 0.64% of patients transiting ED were evaluated and completed counseling, testing and referral. Of these, 15 patients tested positive (2.2%) and 12 (80%) were successfully linked to care.
Lyons, M. S. (*Ann Emerg Med* 2005) [63]	United States, [0.16%], High volume ED°°	*n*=8574 [4-year]	Retrospective observational study	ELISA	Government funding, Supplemental staff	Evaluate the degree to which a targeted HIV screening program can be successful in a low-prevalence setting	n° of newly diagnosed HIV patients	a. 0.7% of patients approached tested positive b. To implement a targeted HIV screening program in a low-prevalence setting is possible, but requires greater resources than in high-prevalence area
Schrantz, S. J. (*Ann Emerg Med* 2011) [61]	United States, [0.20-0.50%], Low volume ED°	*n*=1258 [13-month]	Retrospective observational study	ELISA	Government funding, ED staff	Describe the implementation of a local targeted HIV screening program	1. n° of patients approached, n° of patients tested, n° of newly diagnosed HIV patients linked to care 2. Factor prompting patient selection, changes in testing frequency	1.2% of the total ED visitors were tested. Of these, 2.2% resulted in a new HIV diagnosis, of whom 89% were linked to care. Targeted test might lead to increasing testing even in absence of special resources allocated.

								However, testing frequency decreases with the time.
Haukoos, J. S. (*Ann Emerg Med* 2013) [66]	United States, [0.20-0.50%], High volume ED°°	*n*=58016 [8-month]	Prospective before-after design	Rapid	Government funding, ED staff	Compare targeted HIV screening using Denver HIV Risk Score to non-targeted HIV testing	1. n° of newly diagnosed HIV patients 2. Total HIV diagnosis, CD4 cell count, viral load, successful linkage to care	Targeted HIV testing with Denver HIV Risk Score was strongly associated with new HIV diagnosis when compared to non-targeted screening (1.3% vs 0.2%). The proportion of patients tested into the targeted strategy was only 1/7 of the non-targeted one. Median CD4 cell count was 244 per microliter and 272 per microliter (targeted vs non-targeted). 100% of linkage to care.
Christopoulos, K. A. (*AIDS Patient Care STDS* 2011) [65]	United States, [0.20-0.50%], Low- volume ED°	*n*=5340 [17-month]	Retrospective observational study	Rapid	Government funding, ED staff^^	Evaluate the impact of adding targeted HIV screening to diagnostic testing	1. n° of patients tested, n° of newly diagnosed HIV patients, n° of newly diagnosed HIV patients linked to care 2. Demographics and CD4 cell count	Median number of tests per month and new HIV diagnosis per month significantly increased after the change in testing strategy. 1.2% of patients tested resulted HIV positive. Of these, over 90% were successfully linked to care. Median CD4 cell count 268 per microliter.

§Local HIV-prevalence was tested or estimated
§§Hospital seroprevalence
°ED receiving less than 50.000 patients annually or covering urban area of more less than 600,000 inhabitants
°°50,000 patients annually or covering urban area of more than 600,000 inhabitants
°°°8 EDs in serving the 20% of adult local population
^research nurses, medical students
^^ with supplementary program coordinator
RCT* = randomized controlled study
CRXO** = cluster-randomized crossover trial
CRT*** = cluster-randomized trial
QALYs**** = quality-adjusted life years

Appendix 1 – Search Strategy

MEDLINE Search Strategy (Literature Search performed: 28th Feb 2020):

1. exp HIV infections/ (649450)
2. HIV.mp. (748838)
3. (Target*adj4 (screen* or test*)).mp. (53912)
4. exp Emergency Service, Hospital/ (79814)
5. (A&E or "accident and emergency" or Emergency Department*).mp. (1497590)
6. 1 or 2 (910758)
7. 4 or 5 (1535274)
8. 3 and 6 and 7 (205)

EMBASE Search Strategy (Literature Search performed: 28th Feb 2020):

1. exp Human immunodeficiency virus infection/ (371171)
2. HIV.mp. (748838)
3. (Target*adj4 (screen* or test*)).mp. (53912)
4. emergency ward/ (205262)
5. (A&E or "accident and emergency" or Emergency Department*).mp. (1497590)
6. 1 or 2 (869295)
7. 4 or 5 (1571405)
8. 3 and 6 and 7 (209)

Appendix 2 - List of excluded papers with reason

Targeting HIV testing at a population level: Cost effectiveness of three approaches Ayerbe, C. G.	Study design did not fit with eligibility criteria
Comparison of routine versus targeted HIV testing strategies: Coverage and estimated missed infections in emergency room and primary care centre Elias, M. J. P.	Study design did not fit with eligibility criteria
Cost-effectiveness analysis of universal vs targeted human immunodeficiency virus (HIV) screening approaches to identify new HIV diagnoses in the emergency department (ED) Batista, A. E.	Only abstract for conference
Yield of screening in the ED: Effectiveness versus efficacy Derks, L. S.	Only abstract for conference
HIV risk assessment using longitudinal electronic health records Feller, D.	Only abstract for conference
Incremental cost per newly diagnosed HIV infection (NDHI): Routine (RTS), targeted (TTS), and current clinical practice testing strategies (CPTS) Gomez-Ayerbe, C.	Only abstract for conference
A multi-center pragmatic randomized comparison of HIV screening strategy effectiveness in the emergency department: The HIV tested trial Haukoos, J.	Only abstract for conference
A pragmatic randomized clinical trial of rapid HIV screening in emergency departments Haukoos, J.	Only abstract for conference
Enhanced targeted HIV screening using the denver HIV risk score outperforms nontargeted screening in the emergency department Haukoos, J.	Only abstract for conference
Clinical staff satisfaction of and barriers to targeted and nontargeted opt-out HIV screening in the emergency department: Results from "the HIV tested trial" Haukoos, J.	Only abstract for conference
Effect of rapid HIV screening on emergency departments operational processes and patient throughput: Results from the HIV tested pragmatic randomized effectiveness trial Haukoos, J.	Only abstract for conference
Targeted bedside emergency department HIV screening does not impact length of stay Hernandez, B.	Only abstract for conference
All current emergency department screening strategies for human immunodeficiency virus still leaving many patients undiagnosed	Only abstract for conference

Hsieh, Y. H.	
HIV testing practices and provider attitudes in belize emergency care Wiskel, T.	Only abstract for conference
Screening for HIV: Systematic review to update the 2005 U.S. Preventive Services Task Force recommendation Chou, R.	Review – data already extrapolated
Understanding patient acceptance and refusal of HIV testing in the emergency department Christopoulos, K. A.	Study design did not fit with eligibility criteria
Bundled HIV and Hepatitis C Testing in the Emergency Department: A Randomized Controlled Trial Cowan, E.	Study design did not fit with eligibility criteria
Derivation and validation of the Denver Human Immunodeficiency Virus (HIV) risk score for targeted HIV screening Haukoos, J.	Study design did not fit with eligibility criteria
Risk-based human immunodeficiency virus (HIV) testing fails to detect the majority of HIV-infected persons in medical care Settings Jenkins, T. C.	Study design did not fit with eligibility criteria
Acceptability of HIV Testing Sites Among Rural and Urban African Americans Who Use Cocaine Keith Branham, D.	Limited to specific setting
Missed opportunities for concurrent HIV-STD testing in an academic emergency department Klein, P. W.	Limited to specific setting
The impact of nurse-driven targeted HIV screening in 8 emergency departments: study protocol for the DICI-VIH cluster-randomized two-period crossover trial Leblanc, L. J.	Study design did not fit with eligibility criteria
Effectiveness of nurse-driven HIV screening targeting key populations in emergency departments in metropolitan Paris: The anrs dici-vih cluster-randomized two-period crossover trial Leblanc, L. J.	Only abstract for conference
Relationship of self-reported prior testing history to undiagnosed HIV positivity and HIV risk Lyons, M. S	Study design did not fit with eligibility criteria
Rapid HIV Screening in the Emergency Department Torres, M.	Review – data already extrapolated
Rapid point-of-care HIV testing in youth: A systematic review Turner, S. D.	Review – data could not be extrapolated
Risk, reasons for refusal, and impact of counseling on consent among ED patients declining HIV screening Ubhayakar N.D.	Study design did not fit with eligibility criteria

Rates of emergency department human immunodeficiency virus (HIV) tested in patients tested for sexually transmitted diseases Waxman, M.	Only abstract for conference Limited to specific setting
Influence of an emergency department laboratory order set on rates of HIV and syphilis screening among patients tested for gonorrhea and chlamydia White, D. A. E	Only abstract for conference Limited to specific setting
Missed opportunities for targeted HIV screening and diagnosis among emergency department patients tested for sexually transmitted infections White, D. A. E.	Only abstract for conference Limited to specific setting
HIV screening programs in US emergency departments: a cross-site comparison of structure, process, and outcomes Torres, G. W.	Review – data could not be extrapolated
Feasibility of an emergency department-based, risk-targeted voluntary HIV screening program Kelen, G. D.	Out of study search study time span

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