Targeted HIV screening in the emergency department

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ABSTRACT: 250 words (150 to 250)

Despite considerable improvement in Human Immunodeficiency Virus (HIV) knowledge and treatment in the last three decades, the overall number of People Living with HIV (PLHIV) is still rising with up to one quarter being unaware of their HIV status. Early HIV diagnosis and treatment prolongs life, reduces transmission, improves quality of life and is a cost-effective public health intervention. The Emergency Department (ED) sees a large number of patients from marginalized and traditionally underserved populations in whom HIV is known to be more prevalent and who may not attend traditional services because of either cultural reasons or because of a chaotic lifestyle. This article discusses the two main approaches to screening; 'Opt-out' screening offers testing routinely in all clinical settings, and 'Targeted' screening offers testing to individuals presenting with indicator conditions. There are many studies of 'Opt-out' ED HIV screening in urban areas of high HIV prevalence. However, little is known about the effectiveness of 'targeted' HIV screening especially in areas of low-prevalence. This review discusses the background to HIV screening in the ED and reviews the evidence around 'targeted' HIV screening in adult EDs in different HIV prevalence settings concluding that targeted HIV screening at the ED can be impactful, cost effective and well accepted in the ED population, but its long-term implementation requires extra funding and increased staffing resource limiting its application in low resources setting. Despite most evidence being from areas of high-HIV prevalence, targeted screening might also be appropriate in low-HIV prevalence areas.

Diagnosis of Human Immunodeficiency Virus (HIV)

Since the first HIV cases were reported more than three decades ago, 78 million people have become infected with HIV and 35 million have died from AIDS-related illnesses. Despite considerable improvement in HIV knowledge and treatment HIV is still a public health threat in 2020 and the overall number of People Living with HIV (PLHIV) is still rising[1] with up to one quarter being unaware of their HIV status.[2] 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] Currently, 2019 UNAIDS data shows that of all people with HIV worldwide, 81% knew their HIV status, 67% were accessing antiretroviral treatment and 59% of those on treatment were virally suppressed.[1]

In 2019, there were around 38 million people worldwide with HIV or AIDS (Acquired immunodeficiency syndrome). Of these, 36.2 million were adults and 1.8 million were under 15 years old. AIDS-related deaths have dropped by 60% since the peak in 2004 and in 2019, around 690,000 people died from AIDS-related illnesses worldwide, compared to 1.1 million in 2010. An estimated 1.7 million individuals worldwide acquired HIV in 2019 and although this marked a 23% decline in new HIV infections since 2010, the high burden of HIV infection worldwide and the large proportion of PLHIV (People Living with HIV) unaware of their serostatus means that early HIV detection and wider access to HIV screening represents a crucial public health challenge to urgently overcome.[1,4,5]

Rational for screening

Early diagnosis and treatment for HIV prolongs life, reduces transmission, improves quality of life and has been demonstrated to be a cost-effective public health intervention. Early HIV identification may have a role in prevention of virus transmission from index cases to uninfected people[76,77,6,7] and delayed diagnosis increases the risk of severe complications and premature mortality,[8,9,10] as well as the chance of virus transmission,[11,12,13] ultimately leading to major resource usage and healthcare cost.[14,15,16] HIV screening is therefore key not only for successful treatment but also for infection prevention and of benefit not only to the patient but also to the whole community. In-hospital screening selectively targeting certain groups of patients (i.e. elective surgery, prenatal care) is becoming more common but is limited to those attending these specific facilities [17,18]. In 2007, in order to reduce the harm caused by late presentation, the Chief Medical Officers (CMO) of England,

Wales, Scotland and Northern Ireland called on every UK doctor to improve the detection and diagnosis of HIV in non-HIV specialties.[19]

Screening in the Emergency Department (ED)

It is well accepted that the ED can offer a strategic point of screening for a number of healthcare conditions [20,21,22,23,24,25,26,27,28,29,30,31,32] and screening for disease in the ED is becoming more common with screening for alcohol misuse, smoking and dementia now reasonably widespread. In the UK, similar to many European countries, almost a quarter of the entire country's population attend an ED every year making it a sensible place to introduce an HIV screening program.[33,34] The ED provides round the clock care for groups that are traditionally marginalized and underserved and in whom HIV is known to be more prevalent such as migrants, the homeless and intravenous drugs users. [35,36,37] Routine blood samples are also part of ED clinical care and can be easily used for screening.[38]

Approaches to screening

HIV screening guidelines suggest two main approaches to screening: 'Opt-out' screening aims to test people aged 13 to 64 years in all clinical settings unless they decline, and 'Targeted' screening aims to offer screening to individuals presenting with indicator conditions such as pneumonia in those under 60 years of age.[39,40,41] Although the 'opt-out' approach best detects HIV early in the asymptomatic stage of the infection, it has only been shown to be cost-effective in populations where HIV prevalence is greater than 0.1%.[42] **Table 1** lists the defined indicator conditions for HIV testing.[43] For some of these clinical indicator conditions there is some more detailed European HIV prevalence data available, which is displayed in **Table 2**. [43]

History of opt-out/ non-targeted screening in the ED

'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] In the UK, BHIVA (2008) and NICE (2016) published guidelines for HIV screening in all patients attending the ED in high (2-5/1000) and very high (5 or over/1000) risk areas.[58,59] London with an overall prevalence of HIV of 5.4/1000 was the first city in the UK (England 1.9/1000) to offer non-targeted ED HIV screening. [44] Reports of these experiences showed that non-targeted screening 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.[45,46,47,48,49,50,51,52,53]

Adoption of opt-out/ non-targeted screening in the ED

In light of recommendations issued by national and international agencies, routine opt-out HIV screening has been adopted in some EDs in areas of high-HIV prevalence. [2,54,55,56] High HIV prevalence has been defined as an area with a diagnosed HIV prevalence of between 2 and 5 per 1000 people aged 15 to 59 years (NICE 2016). However, non-targeted screening requires further tests, may include patients previously known to have a HIV positive status, requires dedicated funding to support it and is difficult with EDs currently being overstretched. Concerns persist about its feasibility and effectiveness in the long run especially in setting at lower HIV prevalence.[57,58,59,60,61,62] Recommendations suggest that the HIV seroprevalence rate in the catchment population should be known before any HIV screening program is introduced, and that EDs are not suitable environments for ad hoc opt-out/ non-targeted screening programs in area of low-HIV prevalence or where prevalence rates are uncertain. [53,55]

Targeted screening in the ED

Some national and international agencies suggest any doctor working in the ED should be able to organise and consent a patient for an HIV test and that HIV screening should be performed in the ED setting where it can influence immediate clinical management and improves patient care. However, there are no clear recommendations regarding targeted HIV screening and evidence is sparse about its ED implementation. 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.

Reviewing the evidence for targeted screening in the ED

We conducted a three-concept search to identify papers focusing on targeted HIV screening in the ED using the search terms 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).

The search used the bibliographic databases MEDLINE and EMBASE **[Figure 1]** without any restrictions. Grey literature and unpublished research was also hand-searched using Google Scholar, conference proceedings, ClinicalTrial.gov and OpenGrey. Final search results were exported into EndNote and duplicates removed. Papers were included if they were:

- Peer-reviewed full-text articles
- Published between 2000-2020 (28th February 2020)
- Written in English, French, Spanish or Italian
- 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 3]

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 or comparisons of laboratory techniques

Two authors (OS, BG) independently reviewed the title, abstract and full text of all initially identified publications for relevant articles and disagreements were resolved by consensus and discussion with other reviewers if required. A data-charting form with variables for extraction was developed and data from eligible studies were charted. We collected data on article characteristics (country of origin, study population and sample size), methodology (study design, type of test, funding/staff model, aims/purpose, outcome measure) and key results. A high patient volume ED was defined as more than 50,000 patients annually or covering an urban area greater than 600,000 inhabitants. Study funding was classified as government funding, commercial funding and non-profit foundations (e.g. charities). After removal of duplicates, 241 citations were identified. 197 of these were excluded based on the title and abstract and 44 full-texts were retrieved and assessed for eligibility. Of these, 32 were excluded leaving 12 studies considered eligible for this review [Figure 2] which were grouped by outcomes (impact, feasibility and acceptability) and study designs, measures used and findings and summarised in Table 3.

Evidence for targeted screening in the ED

All papers were published between 2005 and 2019 and study periods varied from 4 months to 6 years. Most studies were from the United States (*n*=8)[60,61,63,64,65,66,67,80] and from areas of high HIV prevalence (*n*=11).[60,61,62,64,65,66,67,68,69,79,80] Those based in Europe (France, Spain and Switzerland) were more recent (2018-2019). 6 studies were performed in high volume EDs.[62,63,64,66,69,80] Study design varied between prospective and retrospective studies, with one third of evidence arising from

RCTs. 3 studies were prospective studies (2 evaluated targeted HIV screening versus diagnostic screening and one compared targeted HIV screening to non-targeted HIV screening).[60,66,79] There were 4 retrospective studies, [61,63,65,80] one cost-utility study [67] and one post-analysis study.[69] All studies were government funded but two were also supported by commercial funding.

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.

Methods of HIV screening

Two different methods of HIV screening were used in the targeted screening studies. Rapid bedside HIV assessment was used in 8 studies, conventional ELISA with confirmatory Western blot was used in 3, and one study used both. In 5 studies, HIV screening was entirely run by ED staff (physicians, nurses, nurse practitioners and social workers).

The impact of targeted HIV screening in the ED

The majority of studies (*n*=8) primarily focused on measures of impact of targeted HIV screening. One study addressed patient acceptability and one addressed program feasibility. The remaining two studies included combined measures of impact/feasibility and impact/acceptability. The primary outcomes of the impact studies were rate of newly diagnosed HIV cases, rate of "early" HIV diagnosis and linkage to care of patients with newly diagnosed HIV.

Rate of newly diagnosed HIV cases

The rate of new HIV cases was the most investigated measure of impact and varied widely (0.03 - 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.[63,64] 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 cluster-randomised crossover trial (CRXO) carried out in France where the number of new HIV diagnoses was compared to a denominator made up all patients approached.[65] 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%. Interestingly, the only study carried out in a low HIV prevalence area (0.16%) reported a rate of new HIV diagnosis (0.7%) still comparable to other studies performed in a high prevalence setting.[63] Test performance may have also differed between studies due to different testing methods used (i.e. rapid bedside HIV assessment or conventional ELISA).

Effect of ED volume on rate of newly diagnosed HIV cases

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 (low volume ED: 1.2, 1.4, 2.2, 2.2 vs high volume ED: 0.7, 0.22, 0.7, 1.3). This may be easily explained by evidence that when ED becomes overstretched, especially in a staff-limited setting, clinical activities are prioritised.[66,67,68,69, 70, 71]

Rate of "early" HIV diagnosis

CD4+ cell count was reported in only two studies. Christopoulos et al reported a median CD4+ cell count at diagnosis of 268 cells/mm^3 in their retrospective study[72] and Haukoos et al reported a median count of 244 cells/mm^3 during their prospective targeted period (versus 272/mm^3 during the non-targeted period).[73]

Cost effectiveness of targeted HIV screening in the ED

Two studies addressed the economics of targeted HIV screening. Dowdy 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. Largely due to it preventing HIV transmission, for every patient tested targeted, screening was shown to save 112 US Dollars.[74] Leblanc et al's CRXO study in multiple EDs in Paris demonstrated an incremental cost per additional new diagnosis of 1324 Euros.[62]

Patient acceptability of targeted HIV screening in the ED

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.[75] 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).[76]

Problems with targeted screening in the ED

Targeted screening increases the likelihood of new HIV diagnoses whilst running fewer tests compared to non-targeted screening but requires actively selecting patients to be offered the test increasing the workload and thought process for busy ED staff. 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 (for equipment and laboratory services).

Requirement for extra staff for targeted screening in the ED

Despite studies comparing targeted vs non-targeted screening showing that targeted screening may lead to fewer tests being performed, and hence being cheaper on the number of assays being performed, additional screening (rather than blanket non-targeted screening) in the ED requires extra staff time.[64,68] Schrantz et al and Leblanc et al found that screening 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.

If targeted screening in the ED 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. Adequate funding must also be available to meet the substantial set-up and staffing costs required for its sustainability. [68]

Requirement for safeguards for targeted screening in the ED

If targeted HIV screening in the ED is planned, other considerations include adoption of a systems-wide approach embedding HIV screening within the governance of the local health system. Effective pathways should be in place including responsibility for those patients returning a positive test in the ED and subsequent contact tracing, which should be undertaken by the local sexual health service and not the ED. Pathways must take into account the 12 week seroconversion period and the risk of

false positive near patient testing. Governance around consent for screening including consideration of the unconscious or incapacitated patient should also be in place.

Clinical bottom line

Regardless of local prevalence rates HIV screening should be offered in the ED to everyone who has not previously been diagnosed with HIV and who is either in a high risk group or has a high risk condition (or symptoms that may indicate HIV). These high risk conditions are also known as indicator conditions and the commonest is pneumonia. ED HIV screening should be offered to all patients with pneumonia under 60 as well as patients with suspected meningitis, lymphadenopathy, cerebral abscess, mononucleosis-like illness, unexplained febrile illness, unexplained persistent blood dyscrasias, oral candidiasis and multidermatomal or severe shingles. High risk groups who have not had recent testing should also be offered screening. These will include sex workers, men who have sex with men, intravenous drug users (IVDUs) and their sexual partners and those having unprotected sexual intercourse or sexual intercourse with individuals from high risk areas (e.g. Sub-Saharan Africa).

Summary of evidence for targeted screening in the ED

Targeted HIV screening at the ED can be impactful, cost effective and well accepted in the ED population, but its long-term implementation requires extra funding and increased staffing resource limiting its application in low resources setting. Despite most evidence being from areas of high-HIV prevalence, targeted screening might also be appropriate in low-HIV prevalence areas. More studies conducted in areas of low HIV prevalence and low and middle-income countries are required. One limitation of this review is its focus on research studies. There may be many EDs across Europe and the rest of the world that have implemented HIV screening (either targeted or non-targeted) and have not reported the findings of their practice. Also, the evidence presented only represents a small [77]proportion of the world, a portion where HIV prevalence is lower than in many low resourced countries where HIV is endemic and Emergency Departments are not well defined. Although examples of non-targeted studies were found in low resourced countries, we are not clear why evidence of targeted HIV screening was not found in these regions. One thought is that emergency type health facilities in these areas are sometimes defined more loosely such as Casualty or Emergency Care Centers. There may also be reports focussed on settings such primary, walk in and urgent care clinics which we were not able to find using our search strategy.

Table and Figure legends:

Figure 1: Targeted screening in the ED Search Strategy.

Figure 2: Targeted screening in the ED literature review flow chart.

Table 1: Definitions of indicator conditions for HIV testing.[43]

Table 2: References for HIV prevalence in patients with clinical indicator conditions in Europe.[43]

Table 3: Summary of evidence around targeted screening in the ED.

Figure 1

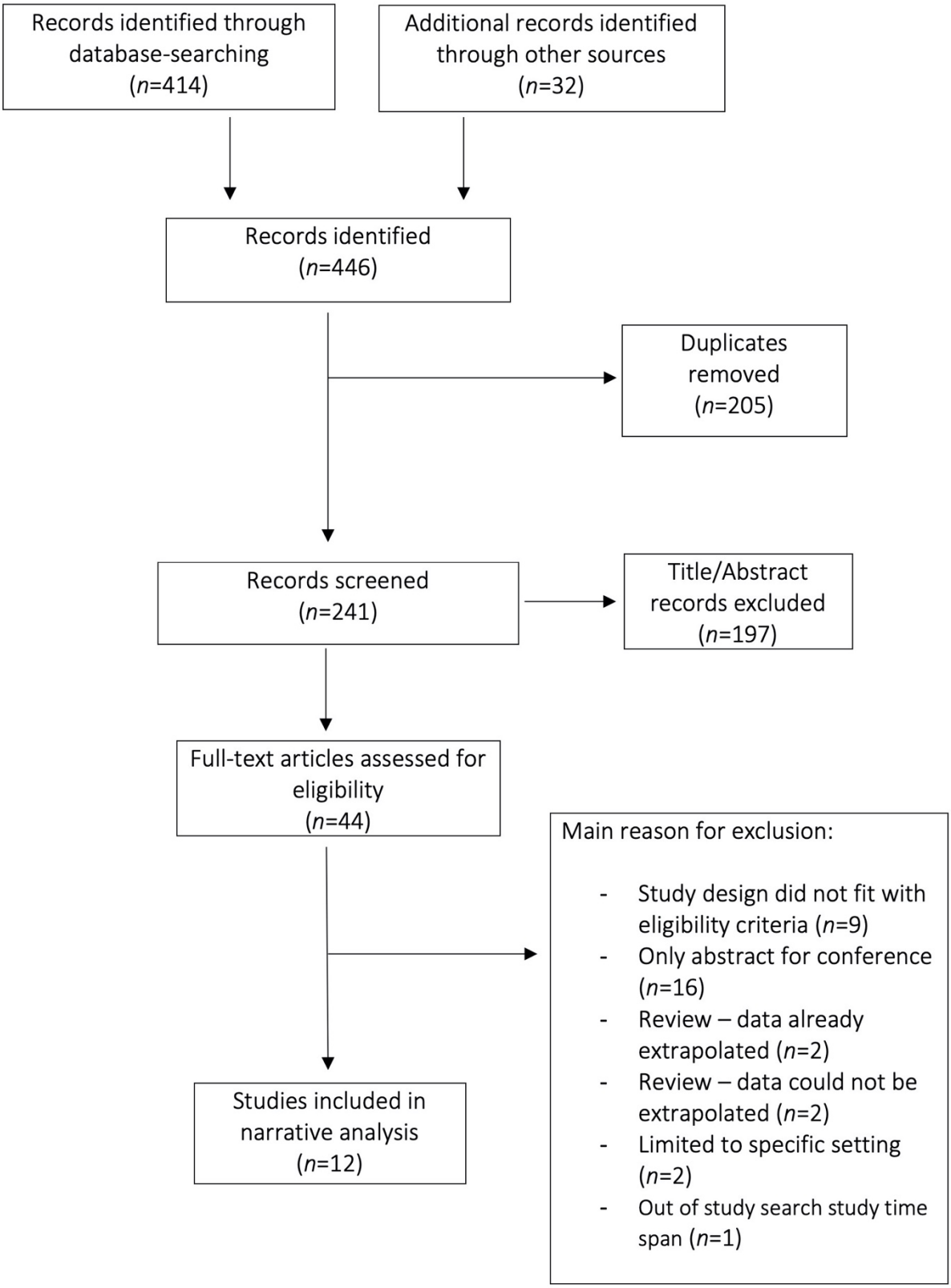
Records identified through database-searching (n=414)
Additional records identified through other sources (n=32)
Records identified (n=446)
Duplicates removed (n=205)
Records screened (n=241)
Title/Abstract records excluded (n=197)
Full-text articles assessed for eligibility (n=44)
Main reason for exclusion:
- 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)
Studies included in narrative analysis (n=12)

Figure 2

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)

Table 1

Potentially AIDS-defining conditions
• Neoplasms (Cervical cancer, Non-Hodgkin lymphoma, Kaposi's sarcoma) • Bacterial infections (Mycobacterium Tuberculosis, Mycobacterium avium complex, Mycobacterium kansasii, other or unidentified Mycobacterium, recurrent Pneumonia; 2 or more episodes in 12 months, recurrent Salmonella septicaemia) • Viral infections (Cytomegalovirus retinitis, other Cytomegalovirus (except liver, spleen, glands), Herpes simplex; ulcer(s) >I month/bronchitis/pneumonitis, Progressive multifocal leucoencephalopathy) • Parasitic infections (Cerebral toxoplasmosis, Cryptosporidiosis diarrhoea >1 month, Isosporiasis >1 month, Atypical disseminated leismaniasis, reactivation of American trypanosomiasis, meningoencephalitis or myocarditis) • Fungal infections (Pneumocystis carinii pneumonia, Candidiasis, oesophageal/bronchial/ tracheal/ lungs, extra-pulmonary Cryptococcosis, disseminated/ extra pulmonary Histoplasmosis, disseminated/ extra pulmonary Coccidiodomycosis, disseminated Penicilliosis)
Conditions in which the prevalence of undiagnosed HIV is more than 0.1%
• Sexually transmitted infections • Malignant lymphoma • Anal cancer/dysplasia • Cervical dysplasia • Herpes zoster • Hepatitis B or C (acute or chronic) • Mononucleosis-like illness • Unexplained leukocytopenia/ thrombocytopenia lasting >4 weeks • Seborrheic dermatitis/exanthema • Invasive pneumococcal disease • Unexplained fever • Candidaemia • Visceral leishmaniasis • Pregnancy (implications for the unborn child)
Conditions likely to have an undiagnosed prevalence of HIV of more than 0.1%
• Primary lung cancer • Lymphocytic meningitis • Oral hairy leukoplakia • Severe or atypical psoriasis • Guillain–Barré syndrome • Mononeuritis • Subcortical dementia • Multiplesclerosis-like disease • Peripheral neuropathy • Unexplained weightloss • Unexplained lymphadenopathy • Unexplained oral candidiasis • Unexplained chronic diarrhoea • Unexplained chronic renal impairment • Hepatitis A • Community-acquired pneumonia • Candidiasis

Table 2

Indicator Conditions for Routine HIV testing	HIV Prevalence
Sexually transmitted infections	4.06%
Malignant lymphoma	0.29 - 2.9%
Anal / cervical cancer/dysplasia	0.37 - 1.6%
Herpes zoster	2.89%
Hepatitis B or C (acute or chronic)	0.36 - 5.7%
Hepatitis C	8 - 59%
Mononucleosis-like illness	3.85 -7%
Unexplained leukocytopenia / thrombocytopenia lasting >4 weeks	3.19%
Seborrheic dermatitis / exanthema	2.06%
Invasive pneumococcal disease	2.4 - 4%
Community-acquired pneumonia (CAP)	0.76%
Candidaemia	6 - 23%
Unexplained fever	3%

Table 3

Author(s), (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
Leblanc J. DICI-VIH[69] 2019	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 higher on weekdays and when research staff participated. Decreased over time and with increased ED volume. b. Patient acceptance increased with research staff participation and decreased over time.
Gomez-Ayerbe C. DRIVE[78] 2019	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. Screening coverage	Rate of newly diagnosed HIV patients and screening coverage significantly higher in the targeted HIV screening program than clinical practice (14/1000 v 6/1000) (1.4%)
Leblanc J. DICI-VIH[62] 2018	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 v 0.8/10.000) (0.03%) (0.7%) b. Incremental cost was 1,324 EU per additional new diagnosis
Gillet C[68] 2018	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. Testing electronic tablets to offer screening 2. Does non-targeted screening increase screening rate	HIV screening rate	a. Screening rate lower in targeted vs non-targeted arm (10 v 48%) b. Acceptance rate did not differ between targeted vs non-targeted arm (48 v 53%)
Lyons MS[64] 2013	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;	a. Proportion of new HIV diagnosis was only slightly lower in targeted vs non-targeted arm (0.22% v 0.31%)

							acceptance rate; risk profile of tested patients; notification rate; n° of newly diagnosed patients linked to care; reasons for declining screening; initial CD4 count in newly diagnosed patients	b. Screening rate was remarkably higher in non-targeted vs targeted arm (40.7% v 29.7%) c. Targeted arm: 66% linkage to care
Haukoos JS[66] 2013	United States, [0.20-0.50%], High volume ED°°	*n*=58,016 [8-month]	Prospective before-after design	Rapid	Government funding, ED staff	Compare targeted HIV screening using Denver HIV Risk Score to non-targeted HIV screening	1. n° of newly diagnosed HIV patients 2. Total HIV diagnosis, CD4 cell count, viral load, successful linkage to care	Targeted HIV screening with Denver HIV Risk Score was strongly associated with new HIV diagnosis when compared to non-targeted screening (1.3% v 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 v non-targeted). 100% of linkage to care.
Dowdy DW[67] 2011	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 US dollars and gained 2.71 QALYs. b. Targeted test prevented ~2.1 HIV transmission events over 16 months
Hudepohl NJ[79] 2011	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 targeted screening program	1. Proportion of patients tested who reported a previous test/had a previous test within the program 2. The cumulative proportion of patients tested in the program	Targeted HIV screening program can have relevant cumulative effects over time since a sizeable proportion of patients returns to the ED more than once (2.6% visits provided with test; 6.9% patients tested)

Schrantz SJ[61] 2011	United States, [0.20-0.50%], Low volume ED°	*n*=1,258 [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 screening 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 screening even in absence of special resources allocated. However, screening frequency decreases over time.
Christopoulos KA[65] 2011	United States, [0.20-0.50%], Low-volume ED°	*n*=5,340 [17-month]	Retrospective observational study	Rapid	Government funding, ED staff^^	Evaluate the impact of adding targeted HIV screening to diagnostic screening	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 tests per month and new HIV diagnosis per month significantly increased after change in screening strategy. 1.2% of patients tested HIV positive. Of these >90% were successfully linked to care. Median CD4 cell count 268 per microliter.
Haukoos JS[60] 2007	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, screening and referral 3. n° of newly diagnosed HIV patients and proportion of these linked to care	Only 0.64% of ED patients were evaluated and completed counselling, screening and referral. Of these, 15 patients tested positive (2.2%) and 12 (80%) were successfully linked to care.
Lyons MS[63] 2005	United States, [0.16%], High volume ED°°	*n*=8,574 [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

§Local HIV-prevalence was tested or estimated; §§Hospital seroprevalence; °ED with <50,000 patients attending annually or covering urban area >600,000 inhabitants; °°50,000 patients annually or covering urban area >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

REFERENCES

[1] Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS data 2018

[2] European Centre for Disease Prevention and Control. Thematic report: continuum of HIV care. Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2017 progress report. Stockholm: ECDC; 2017

[3] 90-90-90: AN AMBITIOUS TREATMENT TARGET TO HELP END THE AIDS EPIDEMIC. UNAIDS. Available at https://www.unaids.org/en/resources/909090

[4] Smith MK, Rutstein SE, Powers KA, Fidler S, Miller WC, Eron JJ Jr, Cohen MS. The detection and management of early HIV infection: a clinical and public health emergency. J Acquir Immune Defic Syndr. 2013 Jul;63 Suppl 2(0 2):S187-99. doi: 10.1097/QAI.0b013e31829871e0. PMID: 23764635; PMCID: PMC4015137.

[5] Rutstein SE, Ananworanich J, Fidler S, Johnson C, Sanders EJ, Sued O, Saez-Cirion A, Pilcher CD, Fraser C, Cohen MS, Vitoria M, Doherty M, Tucker JD. Clinical and public health implications of acute and early HIV detection and treatment: a scoping review. J Int AIDS Soc. 2017 Jun 28;20(1):21579. doi: 10.7448/IAS.20.1.21579. PMID: 28691435; PMCID: PMC5515019.

[6] Kroon EDMB, Phanuphak N, Shattock AJ, Fletcher JLK, Pinyakorn S, Chomchey N, Akapirat S, de Souza MS, Robb ML, Kim JH, van Griensven F, Ananworanich J, Wilson DP. Acute HIV infection detection and immediate treatment estimated to reduce transmission by 89% among men who have sex with men in Bangkok. J Int AIDS Soc. 2017 Jun 28;20(1):21708. doi: 10.7448/IAS.20.1.21708. PMID: 28691441; PMCID: PMC5515043.

[7] Miller WC, Rosenberg NE, Rutstein SE, Powers KA. Role of acute and early HIV infection in the sexual transmission of HIV. Curr Opin HIV AIDS. 2010 Jul;5(4):277-82. doi: 10.1097/COH.0b013e32833a0d3a. PMID: 20543601; PMCID: PMC3130067.

[8] Rodger AJ, Sabin CA. How have guidelines on when to start antiretroviral therapy affected survival of people living with HIV infection? Curr Opin HIV AIDS 2016;11:487–91

[9] Kitahata MM, Gange SJ, Abraham AG, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 2009; 360:1815– 1826.

[10] Grinsztejn B, Hosseinipour MC, Ribaudo HJ, et al. Effects of early versus delayed initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. Lancet Infect Dis 2014; 14:281 – 290.

[11] Miller WC, Powers KA, Smith MK, et al. Community viral load as a measure for assessment of HIV treatment as prevention. Lancet Infect Dis 2013;13:459–64

[12] Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-Manning E, Cottle L, Zhang XC, Makhema J, Mills LA, Panchia R, Faesen S, Eron J, Gallant J, Havlir D, Swindells S, Elharrar V, Burns D, Taha TE, Nielsen-Saines K, Celentano DD, Essex M, Hudelson SE, Redd AD, Fleming TR; HPTN 052 Study Team. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. N Engl J Med. 2016 Sep 1;375(9):830-9. doi: 10.1056/NEJMoa1600693. Epub 2016 Jul 18. PMID: 27424812; PMCID: PMC5049503.

[13] Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Mehendale S, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-

Manning E, Wang L, Makhema J, Mills LA, de Bruyn G, Sanne I, Eron J, Gallant J, Havlir D, Swindells S, Ribaudo H, Elharrar V, Burns D, Taha TE, Nielsen-Saines K, Celentano D, Essex M, Fleming TR; HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011 Aug 11;365(6):493-505. doi: 10.1056/NEJMoa1105243. Epub 2011 Jul 18. PMID: 21767103; PMCID: PMC3200068.

[14] Krentz HB, Auld MC, Gill MJ. The high cost of medical care for patients who present late (CD4<200 cells/microL) with HIV infection. HIV Med. 2004; 5:93–98

[15] Fleishman JA, Yehia BR, Moore RD, Gebo KA; HIV Research Network. The economic burden of late entry into medical care for patients with HIV infection. Med Care. 2010 Dec;48(12):1071-9. doi: 10.1097/MLR.0b013e3181f81c4a. PMID: 21063228; PMCID: PMC3022268.

[16] Levy A, Johnston K, Annemans L, Tramarin A, Montaner J. The impact of disease stage on direct medical costs of HIV management: a review of the international literature. Pharmacoeconomics. 2010;28 Suppl 1:35-47. doi: 10.2165/11587430-000000000-00000. PMID: 21182342.

[17] David R McGowan, Joseph M Norris, Matthew D Smith, Meher Lad. Routine testing for HIV in patients undergoing elective surgery. The Lancet. September 15, 2012 DOI:https://doi.org/10.1016/S0140-6736(12)61537-2

[18] *M J Postma, E J Beck, S Mandalia et al.* Universal HIV screening of pregnant women in England: cost effectiveness analysis. BMJ 1999;318:1656

[19] Chief Medical Officer letter; Improving the detection and diagnosis of HIV in non-HIV specialties, including primary care. September 2007. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_082338.pdf

[20] Ahmad I, Ali PA, Rehman S, Talpur A, Dhingra K. Intimate partner violence screening in emergency department: a rapid review of the literature. J Clin Nurs. 2017 Nov;26(21-22):3271-3285. doi: 10.1111/jocn.13706. Epub 2017 Mar 22. PMID: 28029719.

[21] Boudreaux ED, Camargo CA Jr, Arias SA, Sullivan AF, Allen MH, Goldstein AB, Manton AP, Espinola JA, Miller IW. Improving Suicide Risk Screening and Detection in the Emergency Department. Am J Prev Med. 2016 Apr;50(4):445-453. doi: 10.1016/j.amepre.2015.09.029. Epub 2015 Dec 4. PMID: 26654691; PMCID: PMC4801719.

[22] Hawk K, D'Onofrio G. Emergency department screening and interventions for substance use disorders. Addict Sci Clin Pract. 2018 Aug 6;13(1):18. doi: 10.1186/s13722-018-0117-1. Erratum in: Addict Sci Clin Pract. 2019 Jul 16;14(1):26. PMID: 30078375; PMCID: PMC6077851.

[23] Langerman SD, Badolato GM, Rucker A, Jarvis L, Patel SJ, Goyal MK. Acceptability of Adolescent Social and Behavioral Health Screening in the Emergency Department. J Adolesc Health. 2019 Oct;65(4):543-548. doi: 10.1016/j.jadohealth.2019.05.019. Epub 2019 Jul 31. PMID: 31377163; PMCID: PMC6764595.

[24] Teeuw AH, Kraan RBJ, van Rijn RR, Bossuyt PMM, Heymans HSA. Screening for child abuse using a checklist and physical examinations in the emergency department led to the detection of more cases. Acta Paediatr. 2019 Feb;108(2):300-313. doi: 10.1111/apa.14495. Epub 2018 Aug 14. PMID: 29992712.

[25] Jenkins WD. Chlamydia and gonorrhea screening in the emergency department setting: increasing evidence of utility and need for further research. Am J Emerg Med. 2019 Jun;37(6):1196. doi: 10.1016/j.ajem.2018.10.033. Epub 2018 Oct 18. PMID: 30355478.

[26] White DA, Anderson ES, Pfeil SK, Deering LJ, Todorovic T, Trivedi TK. Hepatitis C Virus Screening and Emergency Department Length of Stay. PLoS One. 2016 Oct 19;11(10):e0164831. doi: 10.1371/journal.pone.0164831. PMID: 27760176; PMCID: PMC5070782.

[27] Adler D, Abar B, Wood N, Bonham A. An Intervention to Increase Uptake of Cervical Cancer Screening Among Emergency Department Patients: Results of a Randomized Pilot Study. J Emerg Med. 2019 Dec;57(6):836-843. doi: 10.1016/j.jemermed.2019.07.021. Epub 2019 Oct 5. PMID: 31594738; PMCID: PMC6904518.

[28] Fallon A, Kilbane L, Briggs R, Dyer A, Nabeel S, McElwaine P, Collins R, Coughlan T, O'Neill D, Ryan D, Kennelly SP. Screening for frailty in older emergency department patients: the utility of the Survey of Health, Ageing and Retirement in Europe Frailty Instrument. QJM. 2018 Mar 1;111(3):151-154. doi: 10.1093/qjmed/hcx242. PMID: 29237068.

[29] Kaltiso SO, Greenbaum VJ, Agarwal M, McCracken C, Zmitrovich A, Harper E, Simon HK. Evaluation of a Screening Tool for Child Sex Trafficking Among Patients With High-Risk Chief Complaints in a Pediatric Emergency Department. Acad Emerg Med. 2018 Nov;25(11):1193-1203. doi: 10.1111/acem.13497. Epub 2018 Oct 31. PMID: 30381877.

[30] Brock C, Yi Y, Papaluca T, Lucas B, Angus PW, Taylor D, Leung C. Exploring the feasibility of targeted chronic hepatitis B screening in the emergency department: A pilot study. Emerg Med Australas. 2018 Dec;30(6):864-866. doi: 10.1111/1742-6723.13118. Epub 2018 Jun 9. PMID: 29885209.

[31] Lappin JM, Ayub MH, Rogers D, Morgan M, Kanyamibwa JY, Shakeshaft A. Routine screening and related interventions significantly improve the effectiveness of emergency department detection and management of alcohol withdrawal syndrome. Emerg Med Australas. 2018 Oct;30(5):648-653. doi: 10.1111/1742-6723.12959. Epub 2018 Mar 12. PMID: 29529713.

[32] Scott RL, Cummings GE, Newburn-Cook C. The feasibility and effectiveness of emergency department based hypertension screening: a systematic review. J Am Acad Nurse Pract. 2011 Sep;23(9):493-500. doi: 10.1111/j.1745-7599.2011.00636.x. Epub 2011 Jun 13. PMID: 21899644.

[33] NHS: London Health Programmes. Quality and Safety Programme Emergency departments: Case for change (http://www.londonhp.nhs.uk/ wp-content/uploads/2013/03/ED-Case-for-change_FINAL-Feb2013.pdf)

[34] Minassian A, Vilke GM and Wilson MP (2013) Frequent emergency department visits are more prevalent in psychiatric, alcohol abuse, and dual diagnosis conditions than in chronic viral illnesses such as hepatitis and human immunodeficiency virus. Journal of Emergency Medicine 45, 520–525

[35] Wu L, et al. (2012) Alcohol and drug use disorders among adults in emergency department settings in the United States. Annals of Emergency Medicine. 60, 172–180.e5

[36] Leaman AM, Rysdale E, Webber R. Use of the emergency department by Polish migrant workers. Emerg Med J. 2006 Dec;23(12):918-9. doi: 10.1136/emj.2006.035980. PMID: 17130598; PMCID: PMC2564252.

[37] Nambiar D, Spelman T, Stoové M, Dietze P. Are People Who Inject Drugs Frequent Users of Emergency Department Services? A Cohort Study (2008-2013). Subst Use Misuse. 2018 Feb 23;53(3):457-465. doi: 10.1080/10826084.2017.1341921. Epub 2017 Oct 16. PMID: 29035611.

[38] Hamill *et al*. (2007) Time to move towards opt-out testing for HIV in the UK. *British Medical Journal.* Vol. 334. pp.1352-1354.

[39] US Preventive Services Task Force. Screening for HIV: Recommendation Statement. Am Family Phys. 2014; 89:666AD

[40] Go¨kengin D, Geretti AM, Begovac J, Palfreeman A, Stevanovic M, Tarasenko O, et al. 2014 European Guideline on HIV testing. Int J STD AIDS. 2014; 25:695–704

[41] HIV in Europe Initiative. HIV Indicator Conditions: Guidance for Implementing HIV Testing in Adults in Health Care Settings. Copenhagen, Copenhagen University, 2015

[42] Hayes R, Sabapathy K, Fidler S. Universal testing and treatment as an HIV prevention strategy: research questions and methods. Curr HIV Res. 2011; 9:429–445

[43] HIV Indicator Conditions: Guidance for Implementing HIV Testing in Adults in Health Care Settings; https://www.eurotest.org/Portals/0/Guidance.pdf.pdf (accessed 11 January 2021)

[44] Public Health England: Future Commissioning of London HIV Prevention Services Project Steering Group. Review of HIV epidemiology in London (https://www.londoncouncils.gov.uk/node/28465)

[45] Bundle Nick, Balasegaram Sooria, Parry Sarah, Ullah Sadna, Harris Ross J, Ahmad Karim, Foster Graham R, Tong Cheuk YW, Orkin Chloe. Seroprevalence and demographic factors associated with hepatitis B, hepatitis C and HIV infection from a hospital emergency department testing programme, London, United Kingdom, 2015 to 2016. Euro Surveill. 2019;24(27):pii=1800377

[46] Cieply L et al (2019). Seroprevalence of HCV, HBV and HIV in two inner-city London emergency departments. Epidemiology and Infection 147, e145, 1–14

[47] Hempling MC, Zielicka-Hardy A, Ellis JP, Majewska W, Fida G. Routine HIV testing in the Emergency Department: feasible and acceptable? Int J STD AIDS. 2016 Dec;27(14):1267-1274. doi: 10.1177/0956462415613727. Epub 2015 Oct 25. PMID: 26503556.

[48] Parry S, Bundle N, Ullah S, Foster GR, Ahmad K, Tong CYW, Balasegaram S, Orkin C. Implementing routine blood-borne virus testing for HCV, HBV and HIV at a London Emergency Department - uncovering the iceberg? Epidemiol Infect. 2018 Jun;146(8):1026-1035. doi: 10.1017/S0950268818000870. Epub 2018 Apr 17. PMID: 29661260.

[49] Bradshaw D, Rae C, Rayment M, Turner N, Turner R, Pickard G, Pillay K, Roberts P, Foxton M, Sullivan AK. HIV/HCV/HBV testing in the emergency department: a feasibility and seroprevalence study. HIV Med. 2018 Feb;19 Suppl 1:52-57. doi: 10.1111/hiv.12590. PMID: 29488696.

[50] Bath R, Ahmad K, Orkin C. Routine HIV testing within the emergency department of a major trauma centre: a pilot study. HIV Med. 2015 May;16(5):326-8. doi: 10.1111/hiv.12216. Epub 2015 Jan 21. PMID: 25604553.

[51] Orkin C, Flanagan S, Wallis E, Ireland G, Dhairyawan R, Fox J, Nandwani R, O'Connell R, Lascar M, Bulman J, Reeves I, Palfreeman A, Foster GR, Ahmad K, Anderson J, Tong CY, Lattimore S. Incorporating HIV/hepatitis B virus/hepatitis C virus combined testing into routine blood tests in nine UK Emergency Departments: the "Going Viral" campaign. HIV Med. 2016 Mar;17(3):222-30. doi: 10.1111/hiv.12364. PMID: 26919291.

[52] Dhairyawan R, O'Connell R, Flanagan S, Wallis E, Orkin C. Linkage to care after routine HIV, hepatitis B & C testing in the emergency department: the 'Going Viral' campaign. Sex Transm Infect. 2016 Nov;92(7):557. doi: 10.1136/sextrans-2016-052742. PMID: 30208368.

[53] Hopkins MJ, Todd S, Beadsworth M, Anderson C, Mohamed Z, Muir D, Vivancos R, Brown AS, Ruf M, Chawla A. Consistent high prevalence of undiagnosed blood-borne virus infection in patients attending large urban emergency departments in England. J Viral Hepat. 2020 Jan;27(1):88-91. doi: 10.1111/jvh.13197. Epub 2019 Oct 1. PMID: 31448490; PMCID: PMC6972612.

[54] Centers for Disease Control and Prevention. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR. 2006; 55:RR-14.

[55] British HIV Association (BHIVA). UK National Guidelines for HIV Testing 2008. BHIVA; 2008

[56] National Institute for Health and Care Excellence (NICE). HIV testing: increasing uptake among people who may have undiagnosed HIV. NICE; 2016

[57] Kecojevic A, Lindsell CJ, Lyons MS, et al. Public Health and Clinical Impact of Increasing Emergency Department-Based HIV Testing: Perspectives From the 2007 Conference of the National Emergency Department HIV Testing Consortium. Ann Emerg Med. Jul; 2011 58(Suppl 1):S151–S159. e151. [PubMed: 21684395]

[58] Irvin, Flagel; Fox. The Emergency Department is Not the Ideal Place for Routine HIV Testing. Ann Emerg Med. 2007; 49(5):722–722. [PubMed: 17452276]

[59] Kelen GD. Public Health Initiatives in the Emergency Department: Not So Good for the Public Health? Academic Emergency Medicine. 2008; 15(2):194–197. [PubMed: 18275451]

[60] Rayment M, Rae C, Ghooloo F, Doku E, Hardie J, Finlay S, Gidwani S, Atkins M, Roberts P, Sullivan AK. Routine HIV testing in the emergency department: tough lessons in sustainability. HIV Med. 2013 Oct;14 Suppl 3:6-9. doi: 10.1111/hiv.12069. PMID: 24033895.

[61] d'Almeida KW, Kierzek G, de Truchis P, Le Vu S, Pateron D, Renaud B, Semaille C, Bousquet V, Simon F, Guillemot D, Lert F, Crémieux AC; Emergency Department HIV-Screening Group. Modest public health impact of nontargeted human immunodeficiency virus screening in 29 emergency departments. Arch Intern Med. 2012 Jan 9;172(1):12-20. doi: 10.1001/archinternmed.2011.535. Epub 2011 Oct 24. PMID: 22025095.

[62] Haukoos JS. The Impact of Nontargeted HIV Screening in Emergency Departments and the Ongoing Need for Targeted Strategies: Comment on "Modest Public Health Impact of Nontargeted Human Immunodeficiency Virus Screening in 29 Emergency Departments". *Arch Intern Med.* 2012;172(1):20–22. doi:10.1001/archinternmed.2011.538

[63] Haukoos JS, Hopkins E, Eliopoulos VT, Byyny RL, Laperriere KA, Mendoza MX, *et al*. Development and implementation of a model to improve identification of patients infected with HIV using diagnostic rapid testing in the emergency department. Acad Emerg Med 2007; 14:1149–1157.

[64] Schrantz, S. J., Babcock, C. A., Theodosis, C., Brown, S., Mercer, S., Pillow, M. T., et al. A targeted, conventional assay, emergency department HIV testing program integrated with existing clinical procedures. *Ann. Emerg. Med* 2011; 58, S85–88e81.

[65] Leblanc J, Hejblum G, Costagliola D, et al.; for the DICI-VIH Group. Targeted HIV screening in eight emergency departments: the DICI-VIH cluster randomized two-period crossover trial. Ann Emerg Med 2018; 10.1016/j.annemergmed.2017.09.011

[66] Hoot NR, Aronsky D. Systematic review of emergency department crowding: causes, effects, and solutions. Ann Emerg Med. 2008 Aug;52(2):126-36. doi: 10.1016/j.annemergmed.2008.03.014. Epub 2008 Apr 23. PMID: 18433933; PMCID: PMC7340358.

[67] Blackburn J, Ousey K, Goodwin E. Information and communication in the emergency department. Int Emerg Nurs. 2019 Jan;42:30-35. doi: 10.1016/j.ienj.2018.07.002. Epub 2018 Aug 17. PMID: 30122462.

[68] McRae AD, Perry JJ, Brehaut J, Brown E, Curran J, Emond M, Hohl C, Taljaard M, Stiell IG. Engaging emergency clinicians in emergency department clinical research. CJEM. 2018 May;20(3):443-447. doi: 10.1017/cem.2017.434. Epub 2018 Jan 30. PMID: 29378670.

[69] Babl FE, Curtis N, Dalziel SR. Review article: A primer for clinical researchers in the emergency department: Part VII. Considering a research higher degree in emergency medicine: How does it work, where to start, what to consider. Emerg Med Australas. 2019 Feb;31(1):4-10. doi: 10.1111/1742-6723.13213. Epub 2018 Dec 11. PMID: 30548155.

[70] Bernstein SL, Aronsky D, Duseji R, et al. The effect of emergency department crowding on clinically oriented outcomes. Acad Emerg Med. 2009; 16: 1–10

[71] Sprivulis PC, DaSilva JA, Jacobs IG, et al. The association between hospital overcrowding and mortality among patients admitted via Western Australian emergency departments. Med J Aust. 2006; 184: 208–112.

[72] Christopoulos KA, Kaplan B, Dowdy D, et al. Testing and linkage to care outcomes for a clinician-initiated rapid HIV testing program in an urban emergency department. AIDS patient care and STDs. 2011 Jul;25(7):439–444.

[73] Haukoos JS, Hopkins E, Bender B, Sasson C, Al-Tayyib AA, Thrun MW. Comparison of Enhanced Targeted Rapid HIV Screening Using the Denver HIV Risk Score to Nontargeted Rapid HIV Screening in the Emergency Department. Ann Emerg Med. 2013 Jan 3

[74] Dowdy DW, Rodriguez RM, Bradley Hare C, Kaplan B. Cost-effectiveness of targeted human immunodeficiency virus screening in an urban emergency department. Acad Emerg Med. 2011;18(7):745–53.

[75] Gillet C, Darling KE, Senn N, Cavassini M, Hugli O. Targeted versus non-targeted HIV testing offered via electronic questionnaire in a Swiss emergency department: a randomized controlled study. PLoS One. 2018;13(3):e0190767.

[76] Leblanc J, Côté J, Pagé MG, Piquet H, Simon T, Crémieux AC; DICI-VIH (Dépistage Infirmier CIblé du VIH) Group. Implementation of Nurse-Driven HIV Screening Targeting Key Populations in Emergency Departments: A Multilevel Analysis From the DICI-VIH Trial. *Worldviews Evid Based Nurs* 2019 Dec;16(6):444-453. doi: 10.1111/wvn.12393. Epub 2019 Sep 2.

[77] Hansoti B, Stead D, Parrish A, Reynolds SJ, Redd AD, Whalen MM, Mvandaba N, Quinn TC. HIV testing in a South African Emergency Department: A missed opportunity. PLoS One. 2018; 13(3): e0193858. doi: 10.1371/journal.pone.0193858

[78] Cristina Gómez-Ayerbe et al. Impact of a structured HIV testing program in a hospital emergency department and a primary care center. PLOS ONE | https://doi.org/10.1371/journal.pone.0220375 August 1, 2019

[79] Hudepohl NJ, Lindsell CJ, Hart KW et al. Effect of an emergency department HIV testing program on the proportion of emergency department patients who have been tested. *Ann Emerg Med* 2011; 58:S140–4.