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Original article

Analysis of the reasons for requesting HIV serology in the emergency department other than those defined in the targeted screening strategy of the “Urgències VIHgila” program and its potential inclusion in a future consensus document



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ABSTRACT

Objective: To describe other reasons for requesting HIV serology in emergency departments (ED) other than the 6 defined in the SEMES-GESIDA consensus document (DC-SEMES-GESIDA) and to analyze whether it would be efficient to include any of them in the future.

Methods: Review of all HIV serologies performed during 2 years in 20 Catalan EDs. Serologies requested for reasons not defined by the DC-SEMES-GESIDA were grouped by common conditions, the prevalence (IC95%) of seropositivity for each condition was calculated, and those whose 95% confidence lower limit was >0.1% were considered efficient. Sensitivity analysis considered that serology would have been performed on 20% of cases attended and the remaining 80% would have been seronegative.

Results: There were 8044 serologies performed for 248 conditions not recommended by DC-SEMES-GESIDA, in 17 there were seropositive, and in 12 the performance of HIV serology would be efficient.

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Palabras clave:

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The highest prevalence of detection corresponded to patients from endemic countries (7.41%, 0.91–24.3), lymphopenia (4.76%, 0.12–23.8), plateletopenia (4.37%, 1.20–10.9), adenopathy (3.45%, 0.42–11.9), meningoencephalitis (3.12%, 0.38–10.8) and drug use (2.50%, 0.68–6.28). Sensitivity analysis confirmed efficiency in 6 of them: endemic country origin, plateletopenia, drug abuse, toxic syndrome, behavioral-confusional disorder-agitation and fever of unknown origin.

Conclusion: The DC-SEMES-GESIDA targeted HIV screening strategy in the ED could efficiently include other circumstances not previously considered; the most cost-effective would be origin from an endemic country, plateletopenia, drug abuse, toxic syndrome, behavioral-confusional-agitation disorder and fever of unknown origin.

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Análisis de los motivos de solicitud de serología del virus de la inmunodeficiencia humana (VIH) en urgencias diferentes a los definidos en la estrategia de detección dirigida del programa “Urgències VIHgila” y su potencial inclusión en un futuro documento de consenso

R E S U M E N

Objetivo: Describir otros motivos de solicitud de serología VIH en servicios de urgencias (SU) diferentes a los 6 definidos en el ellos en el futuro.

Método: Revisión de todas las serologías VIH realizadas durante 2 años en 20 SU catalanes. Las serologías solicitadas por documento de consenso SEMES-GESIDA (DC-SEMES-GESIDA) y analizar si fuera eficiente incluir alguno de motivos no definidos por el DC-SEMES-GESIDA se agruparon por condiciones comunes, se calculó la prevalencia (IC95%) de seropositividad para cada condición, y se consideraron eficientes aquellas cuyo límite inferior del IC95% fue >0,1%. El análisis de sensibilidad consideró que la serología se hubiese realizado solo al 20% de casos atendidos y que el 80% restante hubiese sido seronegativo.

Resultados: Hubo 8.044 serologías realizadas por 248 condiciones no recomendadas por DC-SEMES-GESIDA, en 17 hubo seropositivos, y en 12 la realización de serología VIH resultaría eficiente. La prevalencia más elevada de detección correspondería a pacientes con procedencia de países endémicos (7.41%, 0.91–24.3), linfopenia (4.76%, 0.12–23.8), plaquetopenia (4.37%, 1.20–10.9), adenopatías (3.45%, 0.42–11.9), meningoencefalitis (3.12%, 0.38–10.8) y consumo de drogas (2.50%, 0.68–6.28). El análisis de sensibilidad confirmó eficiencia en 6 de ellas: procedencia de país endémico, plaquetopenia, consumo de drogas de abuso, síndrome tóxico, trastorno conductual-confusional-agitación y fiebre de origen desconocido.

Conclusión: La estrategia de detección dirigida de VIH en SU del DC-SEMES-GESIDA podría incluir eficientemente otras circunstancias previamente no contempladas; la más rentables serían procedencia de país endémico, plaquetopenia, consumo de drogas de abuso, síndrome tóxico, alteración conductual-confusional-agitación y fiebre de origen desconocido.

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Introduction

Human immunodeficiency virus (HIV) infection is a persistent global health problem and in Spain it affects around 150,000 people.¹ One of the main reasons preventing the control of this pandemic is occult infection. Globally, it is estimated that 20% of HIV-infected patients are not aware of their HIV status, a percentage that drops to 13% in Spain^{1,2} and 9% in Catalonia.³ Many of these cases will be diagnosed late, when the CD4 cell count is below 350 per mm³, and this is associated with a poorer prognosis, increased healthcare costs and perpetuation of the transmission of the infection in the population.^{4–6} Therefore, any initiative to increase the diagnosis of HIV infection should be considered of high public health interest. In this regard, there are Spanish and European guidelines^{7,8} of generic application in the practice of medicine that highlight those scenarios in which a request for HIV serology would be more clinically indicated.

From this perspective, attention has been drawn to the opportunity to implement screening strategies for HIV infection in patients being seen at hospital accident and emergency (A&E) departments, given that access to them is universal in many countries. In addition, A&E departments are often the only form of health care for vulnerable groups, in whom the prevalence of HIV infection may be higher than in the general population.^{9–12} Strategies for implementation

have ranged from process-specific screening to universal screening of all patients seen in the A&E department. Relevantly, any strategy is considered cost-effective as long as it achieves a seropositive outcome rate higher than 0.1%.^{13–16}

In line with the targeted process-specific screening strategy, the Infection Group of the Spanish Society of Emergency Medicine (Grupo de Infecciones de la Sociedad Española de Medicina de Urgencias y Emergencias, INFURG-SEMES) and the AIDS Study Group (Grupo de Estudio del Sida, GESIDA) published a consensus document (CD) in 2020 defining targeted HIV screening in the A&E department as good clinical practice in six clinical circumstances with a high prevalence of HIV infection and which are frequent reasons for consultation in A&E: patients consulting for suspected sexually transmitted infection (STI); *chemsex-related* problems; those seeking post-exposure prophylaxis (PEP); those with mononucleosis syndrome; and patients aged 18–65 years with a diagnosis of community-acquired pneumonia or herpes zoster.¹⁷ The “Urgències VIHgila” [Accident and Emergency Departments HIV monitoring] programme in Catalonia and the “Dejatuella” [Leave your mark] programme in the rest of Spain were specifically designed to implement the recommendations of the aforementioned CD,¹⁷ and analysis of their initial results has shown that requesting HIV serology in the six circumstances mentioned above is effective.^{18,19} However, it is possible that there may be other

situations in which requesting HIV serology in A&E may also be effective, although this has not been evaluated to date. Therefore, the main objective of this study was to ascertain the prevalence of seropositivity and assess effectiveness in conditions other than those defined in the CD.

Method

Study design

The “Urgències VIHgila” project was launched by the *Catalan Society of Urgent Medicine and Emergencies (Societat Catalana de Medicina d'Urgències i Emergències, SoCMUE)* in 2021 with the fundamental objective of implementing in A&E departments in Catalonia the recommendations for requesting HIV serology in patients who meet the six conditions defined by the SEMES-GESIDA CD to detect occult HIV infections.¹⁷ The patient was informed of the request for serology and had to consent to it. This verbal consent was recorded in the medical record. The results are updated weekly on a specific open-access website created for this project (www.urgencies-vihgila.cat). The project was implemented in part thanks to a competitive grant from Gilead Sciences. Full details of the project and the creation of the network of “Urgències VIHgila” centres have been published previously.¹⁸

During the period from 1 July 2021 to 30 June 2023 (two years), 20 of the 55 A&E departments in the public healthcare network in Catalonia (36% of the total) joined the “Urgències VIHgila” project, providing care to 5.5 of the 7.9 million inhabitants of Catalonia (70% of the total). The results recorded during this period were used for this analysis.

Variables collected

The total number of HIV serology tests performed in A&E was collected, and whether these requests were made for one of the six circumstances defined in the SEMES-GESIDA CD, or whether they were requested for other circumstances. In the latter case, the main reasons for the request were recorded and collected by the principal investigator of each centre after a weekly review of all serologies performed in their A&E department and their results. With regard to the results, a positive serology test was considered to have detected a new case when there had never previously been a positive serology result or when, despite a diagnosis, the patient had not been followed up in the three years prior to it. These were considered uncontrolled patients and were also included as new cases for the purposes of this study. Two researchers independently grouped individual reasons for requesting HIV serology and formed generic groups of circumstances for HIV serology in A&E. Subsequently, the prevalence of positive serology in each of these groups was analysed. Given the large number of different reasons for request, no preset classification was followed, and cases were grouped on the basis of symptomatological or syndromic similarity. Subsequently, the discordant groupings were discussed between the two investigators and the final classification of each case was agreed upon without knowing the result of the serological test.

Statistical analysis

The prevalence of occult HIV infection for each particular condition was expressed in absolute and relative terms. The latter were obtained by dividing the number of positive cases by the number of tests performed and expressed as percentages with their 95% confidence interval (95% CI). The CI was calculated using the Clopper-Pearson exact binomial method. Tests were considered effective if the lower limit of the 95% CI was greater than 0.1%.^{16,20}

A sensitivity analysis of the prevalence estimates was performed under the assumption that A&E physicians would have biased HIV serology requests to those patients most likely to have undiagnosed HIV infection. This bias could have been induced by other data in the medical history or physical examination suggestive of HIV infection beyond the actual reason for the request. In a previous analysis focusing only on the six circumstances of selective screening for occult HIV infection, it was observed that the percentage of patients with these circumstances who were asked to undergo HIV serology testing ranged from 82% of cases of PEP to 21% of cases of community-acquired pneumonia in patients aged 18–65 years.¹⁹ Therefore, the worst-case scenario was chosen and the sensitivity analysis considered that HIV serology would have been requested in only one out of five patients with the tested circumstance (20%), and that in the remaining cases in which it was not requested (80%) HIV serology would have been negative. Similar to the main analysis, tests were considered to remain effective if the lower limit of the 95% CI of the seroprevalence obtained in this sensitivity analysis remained above 0.1%. This sensitivity analysis was only performed in those conditions where positive cases were detected, as it is not possible to perform sensitivity analyses in those circumstances with no cases (0% prevalence), given that no matter how much the denominator is increased, the numerator will remain 0 and the final prevalence result 0%.

Ethical aspects

As this is an analysis of the results of a programme aimed at improving the quality of care provided in A&E, which evaluates epidemiological data without patient identification, ethics committee approval was not sought. All patients gave their verbal consent for HIV serology as part of their healthcare, both those whose request was in accordance with the six conditions defined in the SEMES-GESIDA CD and those whose request was made for other reasons. While the VIHgila programme is financially supported by industry (Gilead Sciences), the design of this study, the analysis of the results and the drafting of this manuscript were carried out solely by the authors without any involvement of the funder.

Results

Between July 2021 and June 2023 (two years), 14,972 HIV serology tests were performed, with the number of tests per A&E department ranging from 74 to 2672 (median: 535 requests per A&E department, IQR: 275–995 [Table 1]). Of these, 8044 (54%) were requested for 1245 circumstances other than those specified in the SEMES-GESIDA CD (Fig. 1) and formed the basis of this study. The number of serology tests performed under these circumstances per A&E department ranged from 16 to 1478 (median: 208 serology tests, IQR: 126–575) and accounted for 19%–73% (median: 55%, IQR: 37–63) of HIV serologies requested in the A&E department. There were 62 new diagnoses of HIV infection (0.8%) as a result of these requests. The number of HIV-positive serology tests per A&E department ranged from 0 to 9 (median: 2, IQR: 1–5) and the percentage of seropositivity ranged from 0% to 6% (median: 0.9%, IQR: 0.3–1.5) (Table 1).

The 1245 original reasons for requesting the 8044 HIV serology tests were grouped into 248 different circumstances. Table 2 shows them in detail. There were 14 circumstances (207 requests; 2.6%) that actually corresponded to the six situations defined in the SEMES-GESIDA CD that had been initially classified incorrectly, as 13 of them were possibly requested in relation to suspected STIs and one in relation to PEP. In addition, there were five circumstances (1593 requests; 19.8%) where HIV serology was a legal or clinical imperative (emergency dialysis, potential exposure to bio-

Table 1

Total number of serology tests requested and cases detected detailed by hospital and for those requests that were made for circumstances other than the six defined for targeted screening.

	Total HIV serologies N	Positive serologies N (%)	HIV serologies due to circumstances other than targeted screening N (% of total)	Positive serologies N (%)
Hospital Clínic (Barcelona)	2672	25 (0.9)	960 (36)	8 (0.8)
Hospital de Bellvitge (L'Hospitalet de Llobregat, Barcelona)	2491	12 (0.5)	1748 (70)	5 (0.3)
Hospital Vall d'Hebron (Barcelona)	1503	10 (0.7)	993 (66)	4 (0.4)
Hospital de la Santa Creu i Sant Pau (Barcelona)	1083	4 (0.4)	608 (56)	1 (0.2)
Hospital Sant Joan de Déu-Althaia (Manresa, Barcelona)	1083	3 (0.3)	661 (61)	2 (0.3)
Hospital Doctor Josep Trueta (Girona)	733	6 (0.8)	426 (58)	3 (0.7)
Hospital del Mar (Barcelona)	721	10 (1.4)	425 (59)	5 (1.2)
Consorti Sanitari del Maresme (Mataró, Barcelona)	649	10 (1.5)	477 (73)	7 (1.5)
Hospital Parc Taulí (Sabadell, Barcelona)	636	2 (0.3)	137 (22)	2 (1.5)
Hospital de Sant Pau i Santa Tecla (Tarragona)	615	6 (1.0)	390 (63)	3 (0.8)
Fundació Esperit Sant (Santa Coloma de Gramenet, Barcelona)	455	4 (0.9)	123 (27)	2 (1.6)
Hospital Germans Trias i Pujol (Badalona, Barcelona)	446	6 (1.3)	185 (41)	2 (1.1)
Consorti Sanitari de Terrassa (Terrassa, Barcelona)	385	4 (1.0)	204 (53)	2 (1.0)
Hospital Arnau de Vilanova (Lleida)	356	20 (5.6)	149 (42)	9 (6.0)
Hospital Moisès Broggi (Sant Joan Despí, Barcelona)	295	5 (1.7)	213 (72)	3 (1.4)
Hospital Joan XXIII (Tarragona)	268	2 (0.7)	169 (63)	1 (0.6)
Hospital Dos de Maig (Barcelona)	220	4 (1.8)	41 (19)	1 (2.4)
Hospital Verge de la Cinta (Tortosa, Tarragona)	192	3 (1.6)	82 (43)	2 (2.4)
Hospital Municipal de Badalona (Badalona, Barcelona)	95	0 (0)	37 (39)	0 (0)
Hospital de Santa Caterina (Salt, Girona)	74	2 (2.7)	16 (22)	0 (0)
Total	14,972	138 (0.9)	8044 (54)	62 (0.8)

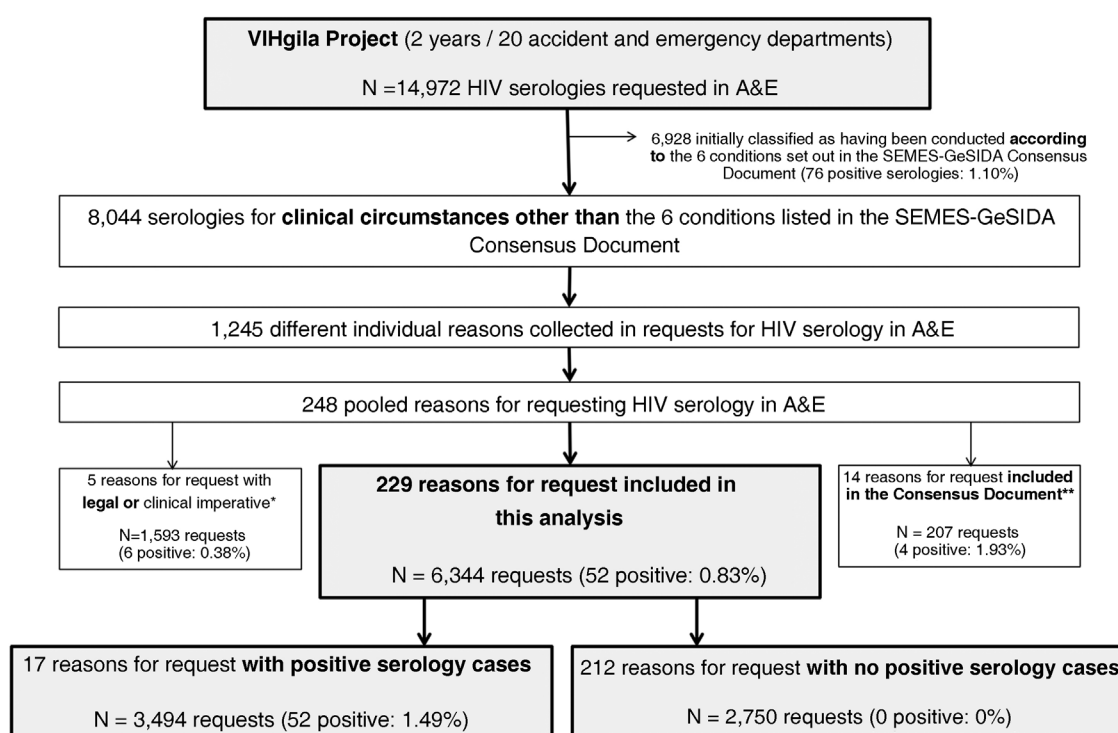


Figure 1. Flowchart of patient inclusion in this study.

logical product, sexual assault, unmonitored pregnancy and organ donation).

Analysis of the potential effectiveness of systematic, targeted screening for occult HIV infection in A&E in the remaining 229 circumstances (6244 requests; 77.6%) showed that in 17 of them (resulting in 3494 HIV serology tests) at least one positive case was detected (Table 2, Fig. 1). The circumstances that generated the most HIV serology tests were fever of unknown origin (796), acute hepatitis (402), non-specific skin lesions (299), behavioural disorder, confusion, agitation or acute psychosis (271) and toxic

syndrome (asthenia, anorexia and weight loss) (205 requests) (Table 2). Conducting HIV serology testing was effective in 12 of these 17 circumstances (Fig. 2), and the highest prevalence of occult HIV infection was in patients from countries with high HIV prevalence (7.41%, 95% CI: 0.91–24.3), lymphopenia (4.76%, 0.12–23.8), thrombocytopaenia (4.37%, 1.20–10.9), adenopathy (3.45%, 0.42–11.9), meningoencephalitis (3.12%, 0.38–10.8) and drug use (2.50%, 0.68–6.28). In addition, the sensitivity analysis, which assumed that in a biased manner, only the 20% of patients with the most suggestive symptoms would have been

Table 2

Distribution (in decreasing order) of the reasons for requesting HIV serology tests classified as different from those included in the “Urgències VIHgila” programme.

	Total requests N = 8044 n (%)	Positive serologies N = 62 n	Positive serologies N = 62 %
<i>17 reasons for request leading to case detection</i>	3494 (43.4)	52	1.488
Fever of unknown origin	796 (9.9)	14	1.759
Hepatitis	402 (5.0)	3	0.746
Non-specific skin lesions (including dermatitis, erythroderma, macules and papules)	299 (3.7)	1	0.334
Behavioural disorder-confusional state-psychomotor agitation (acute psychosis)	271 (3.4)	5	1.845
Toxic syndrome (asthenia, anorexia, weight loss)	205 (2.5)	4	1.951
Focal motor neurological signs	184 (2.3)	1	0.543
Unexplained diarrhoea	162 (2.0)	1	0.617
Recreational drug use or intoxication	160 (2.0)	4	2.500
Risky sexual contact or behaviour (not classified as <i>chemsex</i>)	159 (2.0)	3	1.887
Lesion or inflammation (not purulent) in the oropharyngeal cavity	116 (1.4)	2	1.724
Suspicion of tuberculosis	100 (1.2)	1	1.000
Thrombocytopenia	91 (1.1)	4	4.396
Meningoencephalitis	64 (0.8)	2	3.125
Adenopathy(ies)	58 (0.7)	2	3.448
Oral candidiasis	33 (0.4)	1	3.030
Patient from a country with high prevalence for HIV	27 (0.3)	2	7.407
Lymphopenia	21 (0.3)	1	4.762
No reason stated in the request	346 (4.3)	1	0.289
<i>212 reasons for request that did not lead to case detection</i>	2750 (34.2)	0	–
Hospital staff reviews – general study lab tests	211 (2.6)	0	–
COVID-19 pneumonia	168 (2.1)	0	–
Cytopenias (other than lymphopenia, thrombocytopenia, anaemia)	120 (1.5)	0	–
Acute renal failure	119 (1.5)	0	–
Known or onset psychiatric disorder	100 (1.2)	0	–
Abdominal pain	86 (1.1)	0	–
Urinary tract infection – pyelonephritis	86 (1.1)	0	–
Liver disease-cirrhosis of the liver	68 (0.8)	0	–
Cognitive impairment-Dementia (onset or atypical)	66 (0.8)	0	–
Drug intoxication – self-harm attempt	64 (0.8)	0	–
Sepsis – septic shock	61 (0.8)	0	–
Non-pneumonic lung infection	52 (0.6)	0	–
Musculoskeletal pain or discomfort	52 (0.6)	0	–
Anaemia	51 (0.6)	0	–
Arthritis	51 (0.6)	0	–
Pneumonia in patients >65 years	47 (0.6)	0	–
Diverse neurological symptomatology (aphasia-ataxia-diplopia-dysarthria)	42 (0.5)	0	–
Alcoholism (intoxication or withdrawal syndrome)	42 (0.5)	0	–
Local infection of the skin and subcutaneous tissue	41 (0.5)	0	–
Pericarditis – pericardial effusion	40 (0.5)	0	–
Vasculitis	40 (0.5)	0	–
Heart failure (<i>de novo</i>)	38 (0.5)	0	–
Headache	37 (0.5)	0	–
Pleural effusion	37 (0.5)	0	–
188 other reasons with prevalence <0.5% of requests	999 (12.4)	0	–
<i>5 reasons for request with legal or clinical imperative</i>	1593 (19.8)	6	0.377
Urgent need for dialysis	675 (8.4)	4	0.593
Biological (needlestick, other exposures) occupational or non-occupational accident	618 (7.7)	1	0.162
Sexual assault	197 (2.4)	1	0.508
Pregnant with unmonitored pregnancy	87 (1.1)	0	–
Organ donor	16 (0.2)	0	–
<i>14 reasons for request included in the 6 targeted circumstances already defined</i>	207 (2.6)	4	1.932
Monkeypox (STI)	51 (0.6)	3	5.882
Non-specific orchitis (STI)	44 (0.5)	0	–
Pelvic inflammatory disease (STI)	23 (0.3)	0	–
Proctitis-proctalgia (STI)	16 (0.2)	0	–
Urethritis (STI)	20 (0.2)	0	–
Epididymitis (STI)	15 (0.2)	1	–
Balanitis (STI)	11 (0.1)	0	–
Genital ulcer (STI)	8 (0.1)	0	–
Vulvovaginitis (STI)	8 (0.1)	0	–
6 other reasons with prevalence <0.1% of requests (5 STIs, 1 PEP)	11 (0.1)	0	–

STI: sexually transmitted infection; PEP: post-exposure prophylaxis.

asked to undergo serology testing, confirmed that HIV serology in A&E would still be effective for six of these circumstances: origin from a country with high HIV prevalence (1.48%, 0.18–5.22), thrombocytopenia (0.87%, 0.24–2.11), recreational drug use (0.50%, 0.14–1.27), toxic syndrome (0.39%, 0.11–1.00), behavioural disorder, confusional state, agitation or acute psychosis (0.37%, 0.12–0.86) and fever of unknown origin (0.35%, 0.19–0.59) (Fig. 3).

Finally, of the 212 circumstances in which no positive cases were detected (2750 requests), the most frequent were lab tests of hospital workers or for general study (211), COVID-19 pneumonia (168), other cytopenias apart from lymphopenia, thrombocytopenia or anaemia (i.e., neutropenia or leukopenia) (120), acute renal failure (119) and psychiatric disorder (100) (Table 2).

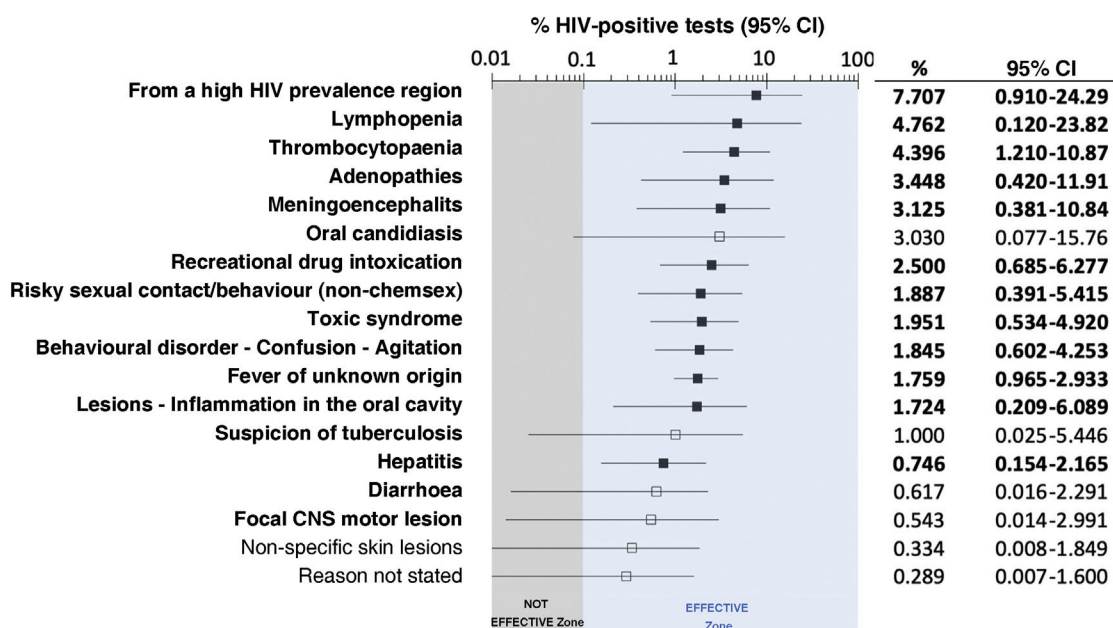


Figure 2. Estimation (in percentages and 95% confidence intervals) of the prevalence of undiagnosed HIV infection in each of the reasons for requesting HIV serology not included in the “Urgències VIHgila” programme’s screening strategy for undiagnosed HIV. The x-axis is expressed in logarithmic format. Bold values denote effectiveness (lower limit of the 95% CI less than 0.1%). CI: confidence interval; CNS: central nervous system.

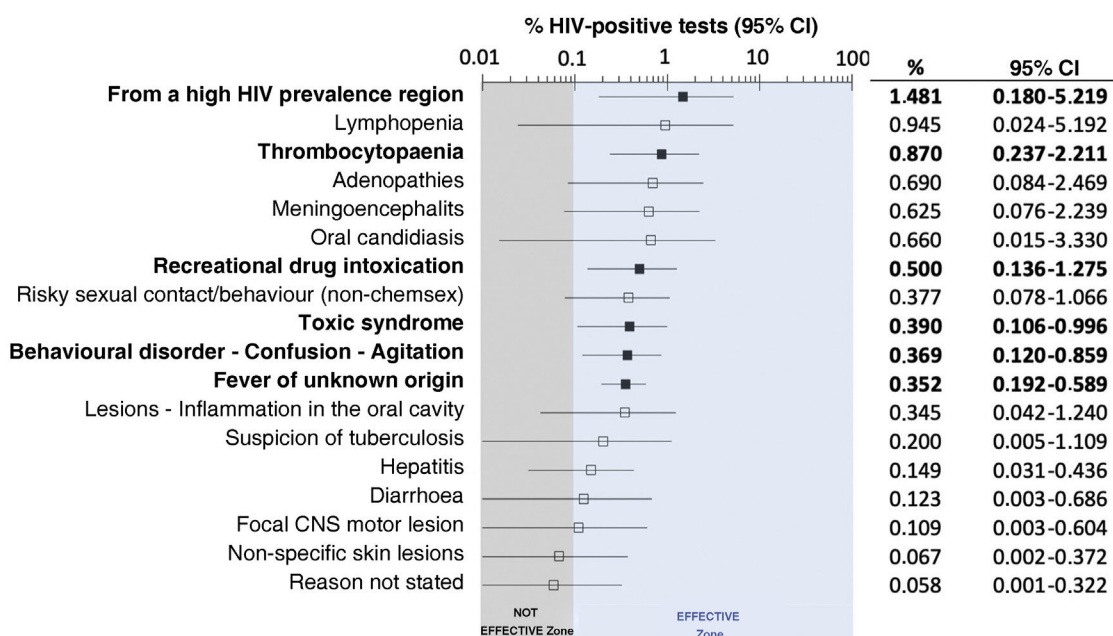


Figure 3. Result of the sensitivity analysis (in which it was considered that HIV serology had been requested from 20% of the patients with the circumstances described and that in the remaining 80% the test would have been negative) showing the estimate (in percentages and 95% confidence intervals) of the prevalence of undiagnosed HIV infection in each of the circumstances not covered by the “Urgències VIHgila” programme’s screening strategy for undiagnosed HIV and for which at least one patient with undiagnosed HIV infection was detected. The x-axis is expressed in logarithmic format. Bold values denote effectiveness (lower limit of the 95% CI less than 0.1%). CI: confidence interval; CNS: central nervous system.

Discussion

This study analyses the circumstances in which HIV serology was requested in A&E departments to detect cases of occult infection in the framework of the “Urgències VIHgila” project. It was found that, in more than half of the cases, HIV serology was requested for circumstances other than the six currently recommended by the SEMES-GESIDA CD. Although this study does not

provide relevant data regarding clinical situations in which the prevalence of HIV infection is increased (all circumstances with positive cases have previously been well defined as increased risk), it is novel in that it analyses – for the first time, we believe – in which of these circumstances screening for HIV infection in A&E can be effective. In this regard, the most important finding is that a number of circumstances have been identified in which such a request would be effective, so that their inclusion in the strategy of

selective screening for HIV infection in A&E could be discussed in the future. Of these, the most obvious and cost-effective would be to request serology testing in patients from countries with high HIV prevalence, with thrombocytopenia, recreational drug use, toxic syndrome, behavioural disorder-confusional state-agitation and fever of unknown origin. These results show concordance and discrepancy with national and European recommendations for requesting HIV serology, which are discussed below.

The Spanish Ministry of Health recommends carrying out HIV serology testing in 30 conditions⁷ with an increased prevalence of HIV infection. These include thrombocytopenia, leukocytopenia, unexplained fever, hepatitis, lymphocytic meningitis and lymphadenopathy, all of which are shown to be effective in this study. On the other hand, other circumstances that are shown to be effective in this study are not covered by these Spanish recommendations, such as recreational drug use, toxic syndrome and behavioural disorder, confusional state, agitation or acute psychosis. With regard to drug use, the recommendations of the Ministry of Health only refer to injecting drug users. However, drug use, especially multiple drug use, is likely to manifest in patients who have greater exposure to practices with increased risk of HIV transmission, either through intravenous drug use or sexual practices.^{21–26} In this regard, the original SEMES-GESIDA CD included *chemsex*, where the most common drugs used are gamma-hydroxybutyrate/gamma-butyrolactone (GHB/GBL), mephedrone, cocaine and methamphetamine, although the use of *poppers* and ketamine is also notable.^{21,22} However, in addition to drug use in the context of *chemsex*, and in view of the present data, patients consulting A&E departments for problems arising from drug use in general (and not related to *chemsex*) may also be considered to be at increased risk of occult HIV infection and should be assessed in a similar way to *chemsex* users. Other recommendations by the Ministry of Health, such as oral candidiasis or diarrhoea, are not effective in our experience, although the recommendations refer to idiopathic oral candidiasis and idiopathic chronic diarrhoea, and it is quite possible that secondary candidiasis (e.g. due to immunosuppression or antibiotics) or acute rather than chronic diarrhoea have also been included in this work. Other conditions included in the Spanish recommendations are more difficult to diagnose in the A&E department, such as candidaemia, tumours or subcortical dementia. Finally, it should be noted that in this study, the request for HIV serology in patients from a high-prevalence country was also effective, and this circumstance is included in the Spanish recommendations, which recommend screening for HIV infection if the prevalence of HIV in that country is higher than 1%.

European recommendations⁸ recommend HIV serology testing in patients with malignant tumours (lymphoma, cervical dysplasia, anal dysplasia or cancer, primary lung cancer), viral infections (mononucleosis, hepatitis B and C), haematological disorders (leukocytopenia, thrombocytopenia, lymphadenopathy), psoriasis (severe dermatological, seborrhoeic) and other circumstances (pneumonia and peripheral neuropathy). Some of these circumstances, such as malignant tumours, are not diagnosed with sufficient certainty in A&E (making them difficult to include as general reasons for screening for HIV infection in this setting), while others, such as psoriasis, are not frequent reasons for A&E visits. In fact, skin diagnoses that were non-specific and grouped in this study as “Non-specific skin lesions” were not effective. On the other hand, mononucleosis and community-acquired pneumonia (in patients aged 18–65 years) are already included in the SEMES-GESIDA CD. Other circumstances, such as hepatitis, adenopathy, lymphopenia and thrombocytopaenia, were effective in the main analysis, but only thrombocytopaenia remained effective in the sensitivity analysis. Therefore, in these circumstances, we cannot rule out the fact that an overly selective request in cases with

other data suggestive of seropositivity may have contributed to this apparent effectiveness. The same applies to requests in patients with meningoencephalitis, which are effective in the main analysis but not in the sensitivity analysis. A re-analysis of all these circumstances in a few years’ time, when the project has accumulated even more experience, will probably provide a more robust answer to this question.

In light of these results, based on the “Urgències VIHgila” programme, which is part of the same philosophy of screening for HIV infection in A&E as the “Dejatuhuella” programme in Spain (both programmes are partially funded by Gilead Sciences), we believe that expanding the number of recommendations in the SEMES-GESIDA CD should be considered. There are undoubtedly missed diagnostic opportunities in A&E in the care of patients with occult infection. In this regard, a previous study on a large population of Spanish A&E departments showed that, of those patients diagnosed *de novo* in these departments, 16% had missed opportunities to be diagnosed in these same A&E departments during the five years prior to diagnosis.²⁷ In this sense, it is a priority to consider including in this CD the request for non-urgent HIV serology in at least six more circumstances—those that demonstrated effectiveness in the main and sensitivity analyses: people from high-prevalence areas; patients with thrombocytopenia; patient with agitation, confusional state or behavioural disorder; toxic syndrome; recreational drug intoxication; and fever of unknown origin—as long as there is no clear aetiological explanation for these circumstances. In addition, six other circumstances can also be considered that may demonstrate the sought-after effectiveness of their routine practice: in patients with adenopathy; meningoencephalitis; risky sexual behaviour or contact (other than *chemsex*); lesions in the oral cavity; lymphopenia; and hepatitis. The first three may be particularly affected, as they were closest to statistical significance in the sensitivity analysis of this study and were those where a type II statistical error is most likely to have occurred. However, extending these circumstances is a new challenge in a complex and highly care-intensive environment such as hospital A&E departments. In fact, a recent publication assessing adherence to the SEMES-GESIDA CD recommendations has shown that adherence is not optimal in several of the circumstances considered.¹⁹ For this reason, we believe that prior to modifying or extending the SEMES-GESIDA CD, there should be a reflection on the feasibility of incorporating a long list of circumstances that may, in actual clinical practice, hinder compliance. In this sense, from the circumstances suggested in this study, it should be decided to incorporate those with greater performance and effectiveness and which are also prevalent reasons for visiting A&E. In addition, this expansion of conditions should be accompanied by electronic tools to facilitate adherence, either through pre-configured requests or through alerts in the electronic health record. This requires not only the involvement of A&E professionals, but also the support of health service managers.

It is important to highlight the fact that the selective screening strategy, on which the “Urgències VIHgila” and “Dejatuhuella” programmes are based, has been shown to be effective and feasible in this and multiple other studies,²⁸ and can lead to significant financial savings for the health system,²⁹ as well as individual benefits for the diagnosed patient and global benefits in terms of public health. Other countries, such as the UK, are moving towards a strategy of universal application to all patients visiting A&E. This universal strategy has not been shown to be more effective than the selective strategy and, in fact, in a country like the UK, with occult infection rates of 5%, it is not effective.¹³ However, it should be noted that there are two major barriers in Spain that could hinder the implementation of selective screening: logistical aspects, due to the high patient caseload of A&E departments; and the need to obtain informed consent for its implementation, which, although

oral, must be recorded in the clinical history, and takes time that is often not available.

Finally, a relevant consideration of this study is that the good results of this model of early HIV diagnosis, which is undoubtedly very cost-effective, have been achieved in a specific geographical area of care, Catalonia, and through collaboration with industry (Gilead Sciences). One of the key positive aspects of the “Urgències VIHgila” programme has been the use of staff external and independent of the centres responsible for supervising the project. It is therefore imperative to convey to the relevant administrations the need for this structure, specifically established for this task, if these results are to be maintained or replicated in other communities or in scenarios in which there is no industry collaboration. Therefore, direct support from the National Health System and the administrations involved is essential if they really want a programme like this to be rolled out across Spain and to be perpetuated over time, as late diagnosis continues to be one of the main causes of the spread of this pandemic in Spain and globally.

Limitations

First, the number of patients with each of the circumstances analysed for whom serology was not requested has not been documented. However, even if this percentage had been 80% and in all of them serology would have been negative, HIV serology would have been effective for six specific circumstances, as shown by the sensitivity analysis performed. Second, the data suggest that some other circumstances may also be effective, although the relatively low number of positive test results or cases may have led to a type II statistical error and we may have considered circumstances to be ineffective that are in fact effective. Third, the different prevalence of unidentified HIV in each autonomous community may make the programme more successful (and therefore more necessary) in high-prevalence communities. As an example, it is worth mentioning that the Hospital Arnau de Vilanova Accident and Emergency Department in Lleida recorded a positive serology rate of 6%, well above the rest of the hospitals. This is probably attributable to the characteristics of the population served, with a high number of seasonal workers during the fruit picking season from countries with a higher prevalence of occult infection than in Spain, and where the chances of being screened for HIV infection are not as widespread as in Spain. Fourth, the willingness of A&E departments to implement a measure (request for HIV serology) that does not have an immediate healthcare impact on the patient's current reason for visiting A&E is important. Catalan A&E departments are among the most willing across the whole of Spain³⁰ and those participating in the “Urgències VIHgila” programme are particularly aware. External validation in other geographical settings is therefore required. In this sense, it should be noted that the findings presented here should be limited to the A&E setting (at other levels of care the prevalence and effectiveness of each of the conditions could be different) and to Catalonia (although in this case, due to the existence of a common public health system in Spain, we believe that it could possibly be extrapolated, at least to the rest of the Spanish autonomous communities). Fifth, only a single reason for the request was collected, which leaves open the possibility of bias on the part of the requesting physician to give more prominence to certain symptoms or syndromes over others. Finally, it is possible that some patients with multiple consultations have undergone more than one test, although prior to the request it is mandatory to check if there are previous serology test results and, in general, serology tests are not repeated if they were carried out during the previous 12 months.

Conclusion

The results of the “Urgències VIHgila” programme, which implements a targeted strategy for detecting patients with occult HIV infection in Catalan A&E departments based on the SEMES-GESIDA CD, show that this strategy could effectively include other circumstances not previously considered. Among them, it seems that it would be highly effective to request HIV serology in patients visiting A&E from countries with high HIV prevalence, thrombocytopenia, recreational drug intoxication, toxic syndrome, behavioural disorder-confusional state-agitation, and fever of unknown origin.

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Authorship

Óscar Miró and Emilia Miró have participated in equal measure in the manuscript and should be considered as first authors.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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