

IC-guided testing in Madrid

# DRIVE 01/02/03 Studies

## Main Findings

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On Behalve of DRIVE study group

# Background

- The revised Centers for Disease Control and Prevention (CDC) guidelines on HIV screening in 2006 recommended **routine HIV testing** in a variety of health care settings. This strategy is cost-effective in populations with HIV prevalence of at least 0.1%<sup>1</sup>.
- In Europe, HIDES studies, supports **Indicator C conditions** guided HIV Testing<sup>2</sup>.
- HIV Testing Spanish Guidelines in 2014 recommended HIV testing in persons with both **HIV risk or Indicator Conditions**<sup>3</sup>

# Objectives

- Exploring more in deep which are **the best strategies** and **settings** for a more extended HIV testing in Spain.
- To evaluate the **prevalence of hidden HIV infection** and prior health care contact in two medical settings: in a Hospital Emergency Room (HER) and in a Primary Care Center (PCC).
- Validate an **HIV Risk practices and clinical conditions questionnaire** (HIV-R-Quest).
- Study HIV positive confirmed patients characteristics and molecular epidemiology.

# Methods

- **Design**: prospective, open label, single arm study.
- **Setting and inclusion period**:
  - Primary Care Center (PCC) García Noblejas (1 September 2012-31 May 2013 **-9 months-**).
  - Hospital Ramón y Cajal Emergency Room (HER) (1 July 2012-31 May 2013 **-11 months-**).

Inclusion criteria	Exclusion criteria
Be attended in HER or PCC	Prior HIV diagnosis
Age 18-60 years old	Prior inclusion in this study
Written informed consent	Not informed consent

# Methods

Interventions were performed with resources provided by the DRIVE study: **rapid test** and **nurses** that performed all procedures of the study.

## Interventions

HIV whole blood rapid  
test (Rapid HIV test)  
**INSTI<sup>®</sup>**

**HIV-Risk Questionnaire/  
3 health care contact questions**

6 Q  
Exposure Risk

**Health care contact  
in the last two years**

HIV testing in the  
last two years

14 Q  
Indicator  
Conditions

**Hospital Emergency Room  
Primary Care Center  
Specialist Physician  
Occupational Health Doctor**

DRIVE 01  
Study

HIV risk of exposure and clinical conditions (RE&CI) questionnaire

HIV		Referring personnel		Project code	
Date of birth (Year)		Gender		Country of Origin	
HIV Anonymous RE&CI questionnaire			HIV Test Result positive/negative		
			YES	No	
1.	Have you ever had intimate sexual intercourse without condom protection which it could represent a risk for acquiring HIV / AIDS in the last 30 years, unless you are with a closed partner?			YES	No
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1.	Have you ever had any of the diseases below?			YES	No
1.	Sexually transmitted infection				
1.	o (Syphilis, Gonorrhea, urethritis, genital herpes, condilomas...)				
1.	o lymphoma				
1.	o Cervical or anal cancer or dysplasia				
1.	o Herpes Zoster				
1.	o Hepatitis B or C				
1.	o Mononucleosis-like Syndrome				
1.	o Thrombocytopenia/Unexplained leucopenia				
1.	o Seborrheic dermatitis				
1.	o Unknown origin/unexplained Fever				
1.	o Repeated oral or vaginal Candidiasis without antibiotic use				
1.	o Oral hairy leukoplakia				
3.	o Unexplained prolonged (>3 months) Diarrhea				
1.	o Unexplained weight loss				
	o Mycobacterium Tuberculosis Disease				

# HIV Rapid Test INSTI®



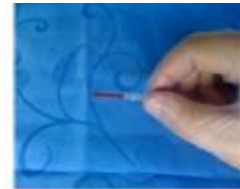
Identificación de la prueba



Pinchazo del dedo



Formar gota grande de sangre



Sangre entra por capilaridad en la pipeta hasta la raya



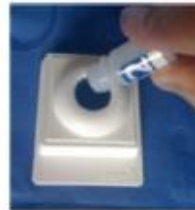
Añadir sangre de la pipeta a la botella 1.



Cerrar botella 1. e invertir dos veces



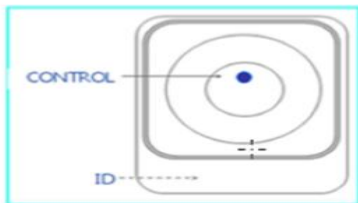
Añadir todo el contenido de botella 1. a la casete



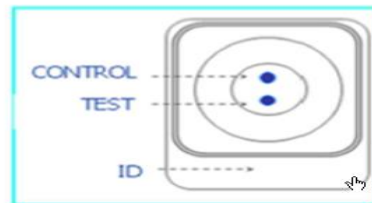
Añadir todo el contenido de botella 2. a la casete



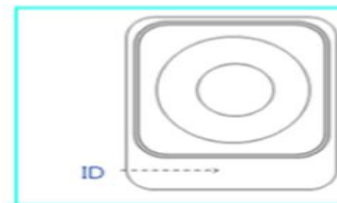
Añadir todo el contenido de botella 3. a la casete



NEGATIVE



POSITIVE



INVALID



All Study procedures were performed by trained nurses, specifically dedicated to explain the study, obtain the informed consent, give the questionnaire and do the test.

# Results

- 5,333 HIV rapid test. 4 tests were eliminated: 2 weak positive tests that were not confirmed and 2 non reactive tests. Final N= 5,329.

Population studied (Paired HIV-test/ER&IC Quest)	
N	5,329
Women	50.36%
Median age years (IQR)	37 (28-47)
Origin	
Spain	74.92%
Latin-America	20.12%
Eastern Europe	2.53%
Africa	0.99%
Western/Center Europe	0.92%
Other Origins	0.51%
Setting	
Primary Care Center	69.3%
Hospital Emergency Room	30.7%

HIV testing in Clinical practice is clearly below what Guidelines recommends

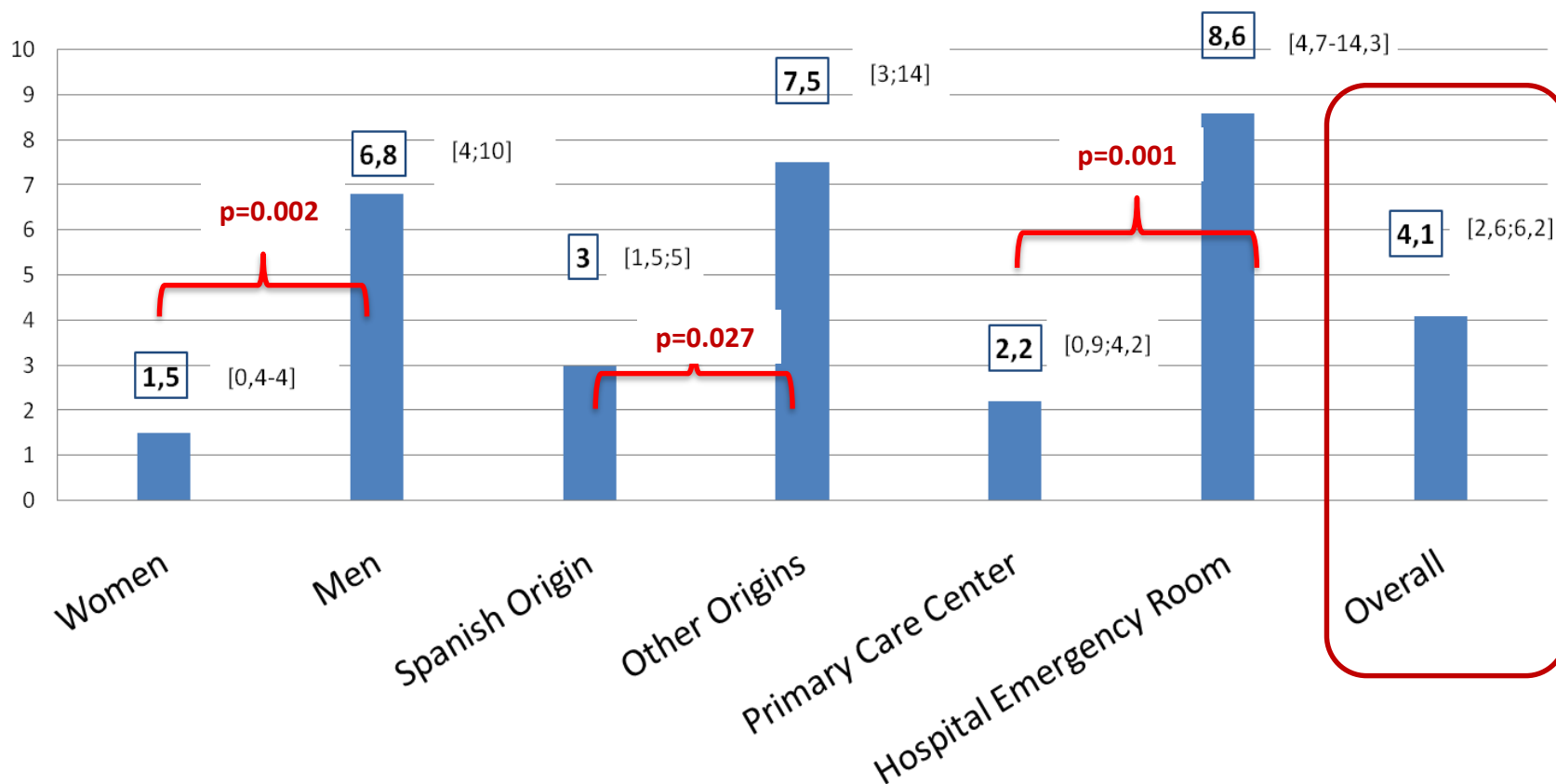
		Emergency Room	Primary Care Center
Settings		Attended Population	
Clinical Practice		63,054	11,220
	2011-2012 Tested Population	210	414
	HIV testing Coverage	0.3 %	3.68 %
	2012-2013 Tested Population	327	367
	HIV testing Coverage	0.51 %	3.27 %
	2013-2014 Tested Population	429	404
		0.68 %	3.6 %
DRIVE	2012-2013 Tested Population	1,635	3,694
	HIV testing Coverage	2.59 %	32.9 %

## Number of New HIV Diagnosis Comparison with clinical practice

		Hospital Emergency Department	Primary Care Centre	Overall
Clinical Practice 2011-2012	Tested Population	210	414	624
	NHID rate	(0) 0 ‰	(1) 2.41 ‰	(1) 1.6 ‰
Clinical Practice 2012-2013	Tested Population	327	367	695
	NHID rate	(3) 9.1 ‰	(0) 0 ‰	(3) 4.3 ‰
Clinical Practice 2013-2014	Tested Population	429	404	833
	NHID rate	(3) 7 ‰	(0) 0 ‰	(3) 3.6 ‰
DRIVE 2012-2013	Tested Population	1,635	3,694	5,329
	NHID rate	(14) 8.6 ‰ (4.7-14.3)	(8) 2.2 ‰ (0.9-4.2)	(22) 4.1 ‰ (2.6‰-6.2‰)

# Results

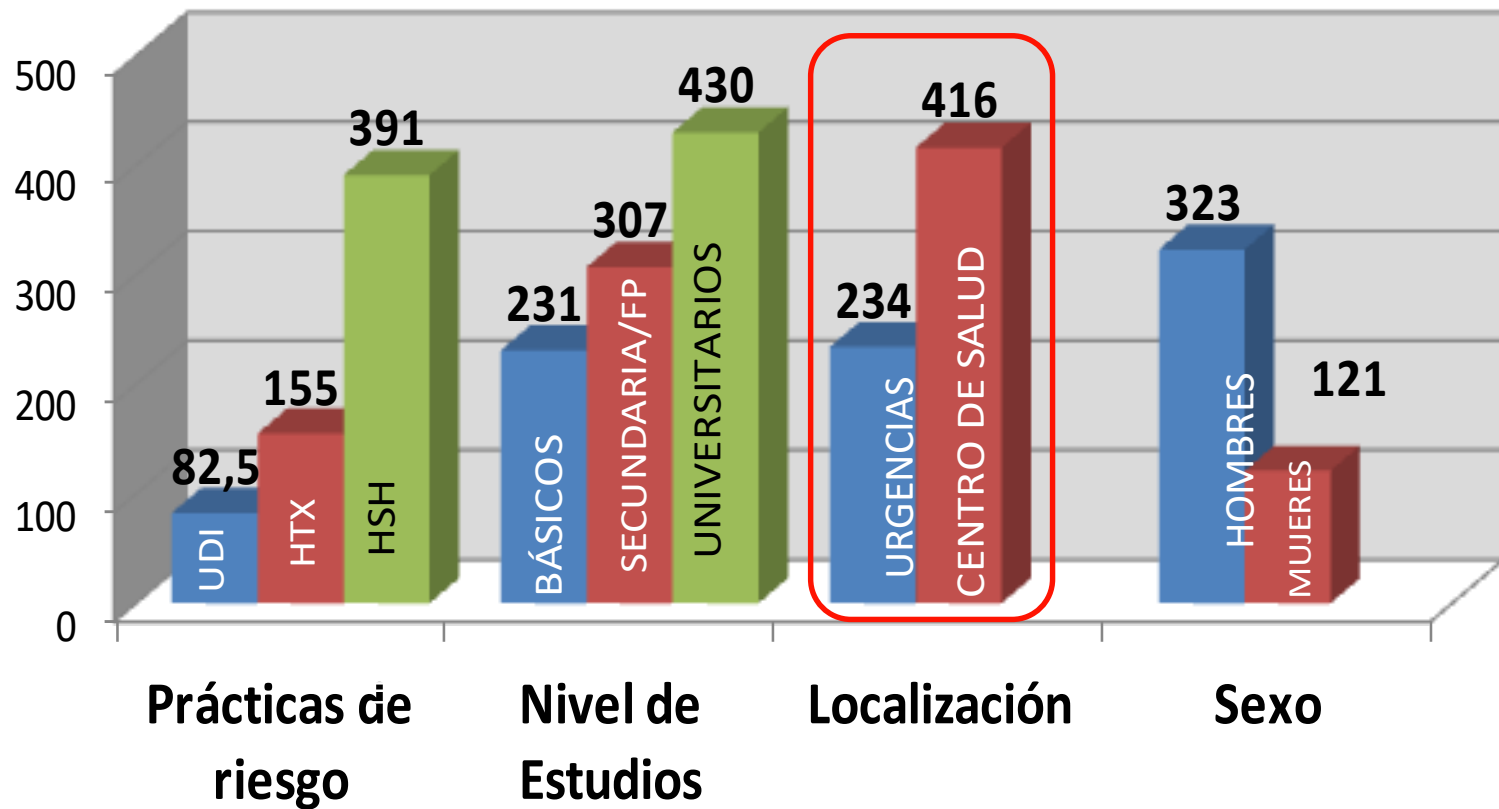
## Prevalence of HIV Hidden Infection x1000 Patients Included in DRIVE Study: According to Sex, Origin and Setting



A significant late HIV diagnosis was observed.

- Mean CD4 cell count at Diagnosis, and % <350 cell count

**CD4<350 57 %**



# Health Care Contact According to HIV Rapid Test Result

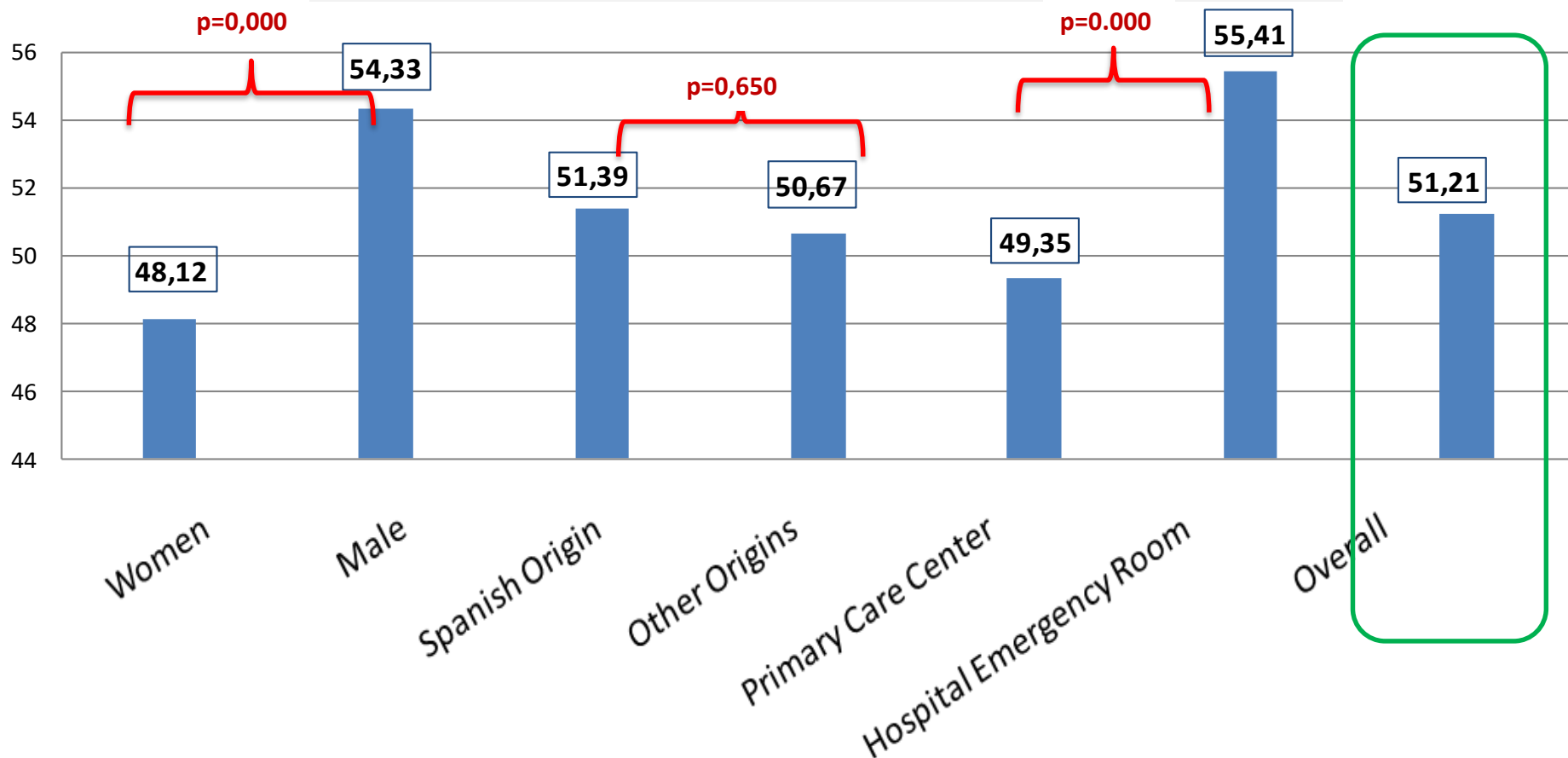
Health Care Contact (N= 5,331)		Overall	Negative	Positive	P
Any Health contact in last two years	Yes (%)	94.4	94.4	90.9	0.478
Hospital Emergency Room	Yes (%)	46.5	46.4	55	0.443
Primary Care Center	Yes (%)	91	91	70	0.001
Specialist Physician	Yes (%)	39.9	40	35	0.648
Occupational Health Physician	Yes (%)	11.3	11.4	0	0.109
Number of Health care contacts	Mean ±SD	8.9±0.15	8.9±0.15	8.1± 1.9	0.71
Prior HIV testing	Yes (%)	29.9	29.7	59.1	0.003
			(OR: 3.4, 95% CI: 1.5-8.02)		

Estimation of Missed Opportunities for HIV diagnosis:

90.9%-59.1%=**31.8%**

# Results

## Percentage of Patients with an HIV Risk Practice and/or clinical condition positive Questionnaire in DRIVE Study: According to Sex, Origin and Setting



**TABLE 2.** Unadjusted and adjusted analyses of HIV RE&IC questionnaire items comparing yes answers between HIV diagnosed individuals and non-HIV-infected

	UOR	IC 95 %	P	AOR*	IC 95 %	P
Risk exposure items						
Unprotected sexual intercourse	7.37	2.713–19.99	<0.001	5.733	2.08–15.72	0.001
Partner with HIV infection	26.5	10.9–69.66	<0.001	30.88	11.33–84.162	<0.001
Man with man sex	29.13	12.443–68.177	<0.001	24.47	11.06–63.47	<0.001
To have received any hemoderivative transfusion	2.43	0.32–18.23	0.37	2.95	0.34–19.62	0.34
Parental illicit or recreational drug use <sup>‡</sup>	12.84	2.90–56.74	<0.001	14.192	3.03–66.46	0.001
Any suspicion of HIV acquisition <sup>‡</sup>	4.45	1.91–10.32	<0.001	3.83	1.64–8.94	0.002
Clinical conditions items						
Sexually transmitted infection	6.632	2.5–17.08	<0.001	4.95	1.88–13.00	0.001
Lymphoma	1.00	0.99–1.00	0.790	0	0–0	0.79
Cancer	1.00	0.99–1.00	0.69	0	0–0	0.77
Herpes Zoster	10.87	4.20–28.11	<0.001	15.17	5.58–41.22	0.002
Mononucleosis-like syndrome	3.98	0.92–17.21	0.102	4.89	1.1–21.70	0.037
B or C hepatitis	9.38	3.6–24.22	<0.001	8.88	3.40–23.21	<0.001
Trombopenia	11.44	1.47–88	0.003	16.81	2.05–137.91	0.009
Seborrheic dermatitis	5.14	1.50–17.56	0.004	7.16	2.0025.62	0.002
Candidiasis oral	3.092	1.35–8.418	0.02	6.48	2.24–18.77	0.001
Oral hairy leukoplakia	1.00	0.99–1.00	0.85	0.00	0.00	0.89
Unexplained fever	3.81	0.89–16.55	0.053	4.09	0.93–17.87	0.061
Unexplained prolonged diarrhea (>3 months)	16.601	4.71–57.89	<0.001	18.53	5.15–66.65	<0.001
Unexplained weight loss <sup>‡</sup>	21.0	8.43–52.65	<0.001	21.59	8.49–54.87	<0.001
Mycobacterium tuberculosis disease	3.84	0.50–28.98	0.24	3.35	0.438–25.62	0.244

AOR = adjusted odds ratio, IC = indicator conditions, UOR = unadjusted odds ratio.

\* Adjusted by/for sex, age, country of birth, and health setting of inclusion.

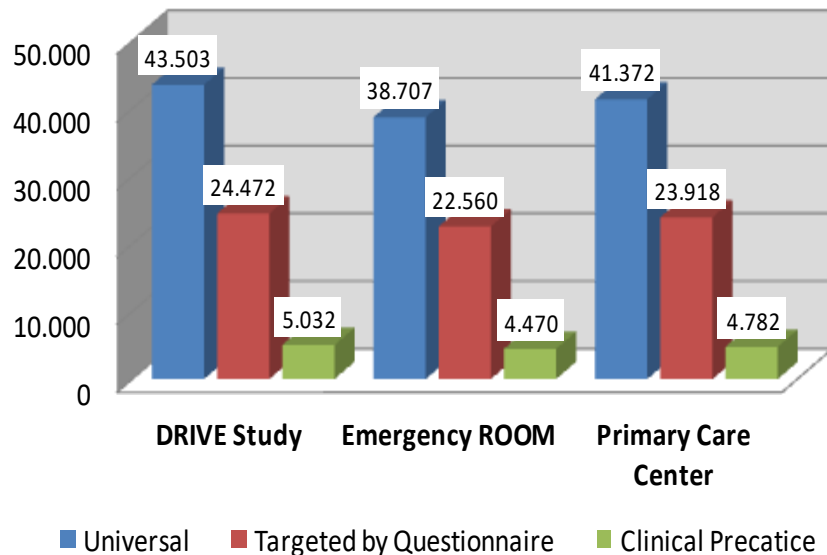
## HIV RISK and Indicator Conditions Questionnaire

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Overall Questionnaire ER&IC			
<b>100% (84,6%-100%)</b>	49% (47,7%-50,4%)	0,80% (0,50%-1,22%)	<b>100% (99,9%-100%)</b>
Risk practice Quest			
<b>86,4%</b> (65%-97%)	61,3% (60%-62,6%)	0,92% (0,55%-1,43%)	<b>99,9%</b> (99,7%-100%)
Indicator Conditions Quest			
<b>91%</b> (70,8%-98,9%)	74,4% (73,2%-75,6%)	1,45% (0,88%-2,23%)	<b>99,9%</b> (99,8%-100%)

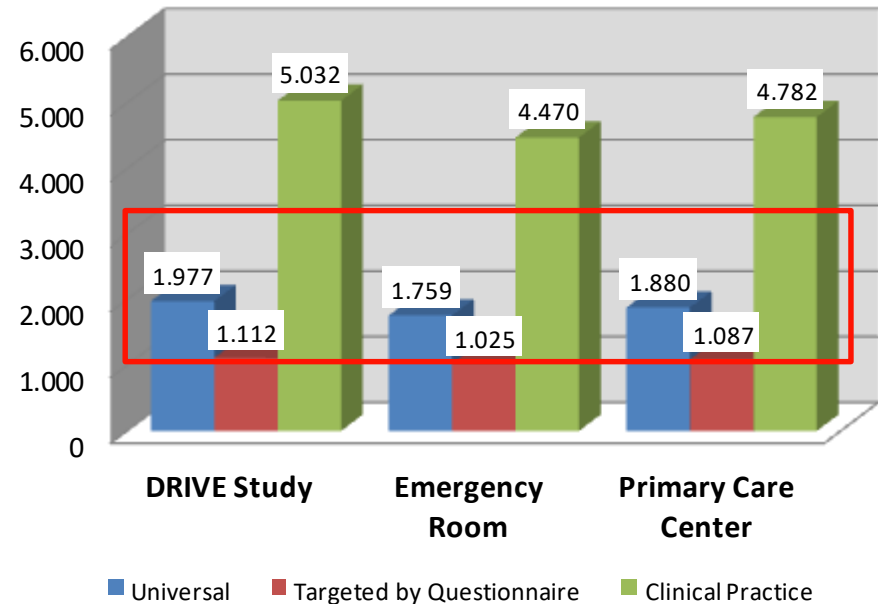
# Costs associated with different strategies

- From a health care perspective, using direct costs and Euros currency, we calculated overall budget and incremental cost per New HIV Diagnosis
- Unitary costs considered were: HIV Rapid Test, nurse, registry, transport and HIV confirmation when necessary.

**Overall Cost (€) according to the strategy and setting**



**Cost per New HIV Diagnosis**



The lowest overall Budget is found In clinical Practice.  
However the cost associated with any New HIV Diagnosis is lower in DRIVE study,  
and even lower when only Questionnaire positive patients were tested

# Targeting HIV Testing at a population level: Cost-effectiveness of three Approaches

## Diseño DRIVE 01:

- ✓ DRIVE 01 Study is a non-Targeted HIV Testing Programme performed in Emergency Department and Primary Care Centre (PCC).
- ✓ All participants were tested for HIV (Rapid Test) and filled out the self administered RE&CI-Questionnaire.

## Three strategies compared

Quest  
ER&IC

Denver  
Score  
(DHRS)

14  
Indicator  
Conditions  
HIDES

Fecha Prueba	Médico Beneficiario	Código proyecto
Fecha nacimiento	Sexo	País de Origen (desplegable países)
Cuestionario Anónimo		
Resultado Prueba		positivo/negativo
		Si No
1. Ha tenido/Tiene relaciones sexuales en los últimos 30 días que hayan comportado algún riesgo para adquirir la infección por VIH (uso de una pareja no errada sin uso de preservativo siempre o múltiples parejas sin uso de preservativo siempre).		
2. Ha tenido/tiene pareja con infección por VIH.		
3. Ha tenido/tiene relaciones homosexuales.		
4. Le han transfundido.		
5. Ha usado.		
6. (C)		
7. Herpes zoster.		
8. Hepatitis B/C.		
9. Sífilis/Mononucleosis.		
10. Trombopenia/Linfopenia inexplicada.		
11. Dermatitis Seborreica.		
12. Fiebre no explicada.		
13. Candidiasis oral o vaginal de repetición sin toma de antibióticos.		
14. Leucoplasia velosa oral.		
15. Diarrea prolongada (>3 meses) no explicada.		
16. Pérdida de peso no explicada.		
17. Tuberculosis.		
18. Ha acudido a algún centro sanitario en los dos últimos años (urgencias, médico de cabecera, especialistas, médico del trabajo...).		
19. Cuántas veces en los dos últimos años.		
20. Se ha realizado el test de VIH previamente.		
		Fecha

≥ 1  
affirmative  
answer

Variable	Score
<u>Age</u>	
<22 or >60 years	0
22-25 or 55-60 years	+4
26-32 or 47-54 years	+10
33-46 years	+12
<u>Gender</u>	
Male	+3
Other	0
White	0
<u>Sexual Practices</u>	
Sex with a male	+22
Vaginal intercourse	-10
Receptive anal intercourse	+8
<u>Other Risks</u>	
Injection drug use	+9
Past HIV test	-4

DHRS > 30

- Infecciones de transmisión sexual
- Linfoma maligno
- Cáncer/displasia anal
- Displasia cervical
- Herpes zóster
- Hepatitis B
- Sífilis
- Enfermedad
- Fiebre sin causa aparente
- Candidemia
- Leishmaniosis visceral
- Gestación (implicaciones para el feto)

At least one  
Indicator  
Condition

- We calculated **Sensitivity (Sn), Specificity (Sp), Positive Predictive Value (PPV) and Negative Predictive Value (NPV)** of the three tools, considering the gold standard confirmed cases of HIV Infection with EIA/WB
- **Number of Missed HIV Infections (MHI), Test avoided and number of test to obtain a positive result were calculated**
- **Provider perspective directed costs of HIV testing and confirmation plus RP&CC questionnaire were considered to calculate Incremental costs/effectiveness ratio.**

# Results and Conclusions

## Accuracy of three HIV Targeted Testing Strategies: RE&CI Questionnaire, Denver HIV Risk Score and 14 IC of HIDES Study

	Sn	Sp	PPV	NPV	NHD/MHI	Number of test avoided	Number of test to obtain one positive
Non-Targeted Strategy					22/0	0	242
RE&CI Questionnaire	100% (84.6-100%)	49% (47.7-50.4%)	0.80% (0.5-1.2%)	100% (99.9-100%)	22/0	2,601	124
DHRS	72.7%	60.41%	0.76%	99.8%	16/6	3,212	132
14 IC of HIDES	70.8-98.9%	73.2-75.6%	0.88-2.2%	99.8-100%	22/0	2,601	124

If we consider the budgetary impact, the two more diagnoses that are made in DRIVE01 would cost 5388 Euros each.

All three tools avoided HIV Tests, but only the **RE&CI Questionnaire** captured all HIV-Infected subjects detected by the non-targeted strategy.

A selection of HIDES list presented a high sensitivity, and was able to avoid the highest number of tests.

Cost of each NHD obtained using RE&CI-Questionnaire compared to HIDES list is low with respect to the benefit obtained

# Main findings

- With the same work plan, design and resources, HIV routine testing reached higher rate of coverage in Primary Care Center, and patients were diagnosed with higher CD4 cell count.
- The **high prevalence** of hidden HIV infection found in our routine voluntary study (0.41%) supports the implementation of a more extended HIV screening strategy.
- Missed opportunities for HIV diagnosis were observed in almost **one third** of our population.
- Half of the population studied reported risk practice and/or indicator conditions when investigated exhaustively.

# Main findings

- Prior HIV testing frequency was higher in those who finally resulted HIV infected.
- HIV RE&IC self questionnaire accurately discriminated all non- HIV-infected people without missing any HIV diagnoses in a low medium HIV infection prevalence areas.
- Guide HIV Testing by a questionnaire of HIV Exposure Risk and Indicator Conditions, saves costs, without missing New HIV Diagnoses.
- In our Health Area, Guide HIV Testing by a questionnaire of HIV Exposure Risk and Indicator Conditions works better than other tools to find NHIVD

# Thanks and Acknowledgments

## DRIVE GROUP

### Diagnóstico Rápido de la Infección por VIH/SIDA en España

We are grateful to all the patients included in the study.

**Principal Investigator** M<sup>a</sup> Jesús Pérez Elías; **Statistician** Alfonso Muriel; **Help to the design** M<sup>a</sup> Martinez-Colubi, **coordinate the study** C Gómez Ayerbe.

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