
“Detección precoz del VIH”.

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**I Curso de Actualización
en Infección por VIH
para Personal Sanitario
de Atención Primaria**



DETECCION DEL PROBLEMA

- ▶ Hay una proporción elevada de pacientes infectados por VIH no diagnosticados (**EPIDEMIA OCULTA**)
- ▶ Esto conlleva una serie de problemas:
 - Aumento de transmisión por parte de las personas que no conocen si están infectadas
 - Presentación tardía de la infección por VIH (mayor mortalidad)
 - Dificultades de controlar la epidemia
- ▶ Habría que buscar estrategias de diagnóstico precoz



Fracción no Diagnosticada. Región Europea OMS

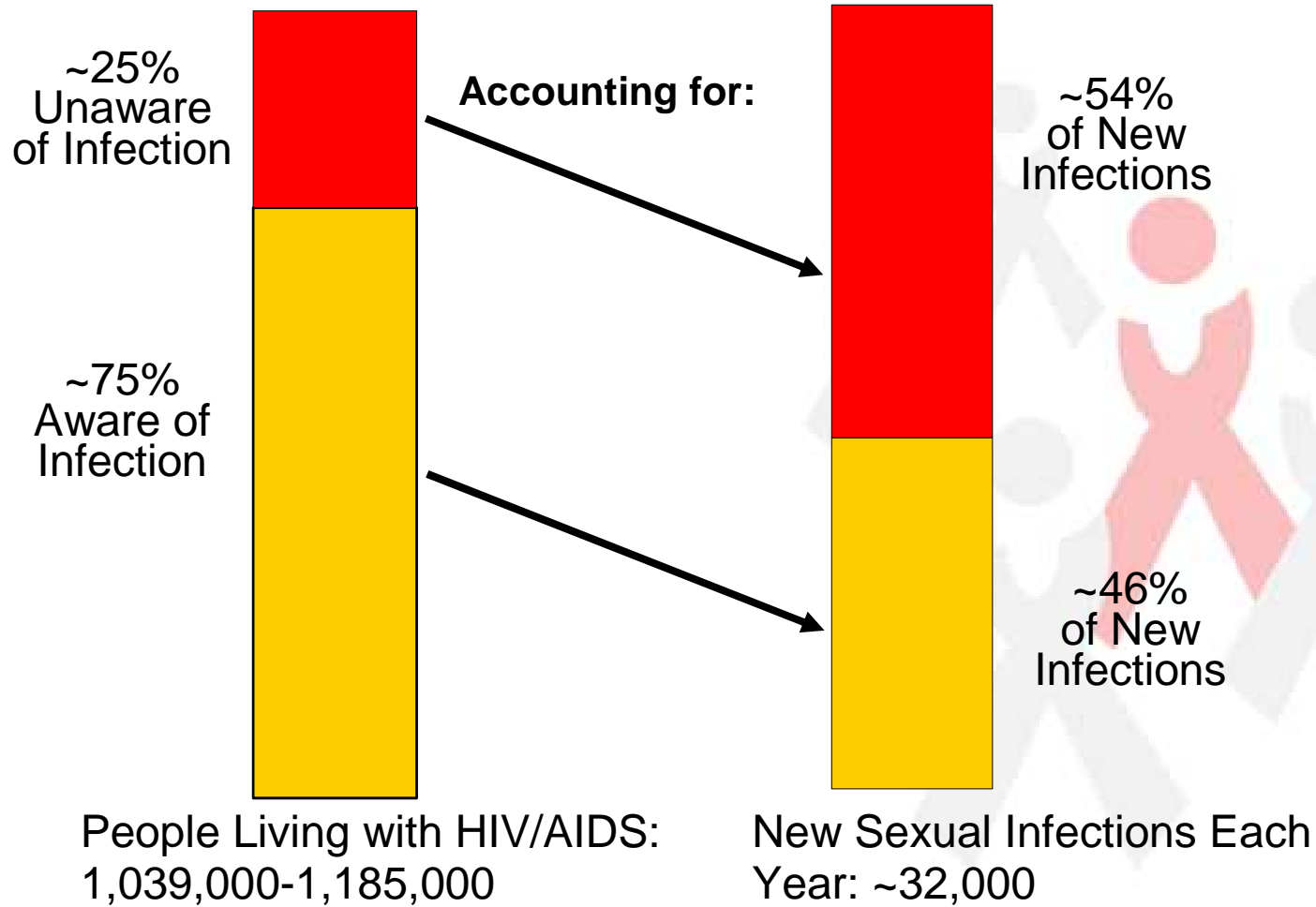
Country	Estimated % of persons living with HIV unaware of their infection
Czech Republic	20-25%
Denmark	15-20%
France	30%
Germany	25-30%
Italy	25%
Latvia	50%
The Netherlands	40%
Poland	>50%
Slovakia	20-30%
Spain	30%
Sweden	12-20%
United Kingdom	30%
Norway	15%
TOTAL EU	30%
TOTAL EU +EEA/EFTA	30%
WHO-EUROPE excluding EU and EEA/EFTA	65%
TOTAL	50%

* Resto de países (38) sin información

Modificado de: Hamers FF et al. HIV Medicine 2008; 9 (Supl. 2):6-12



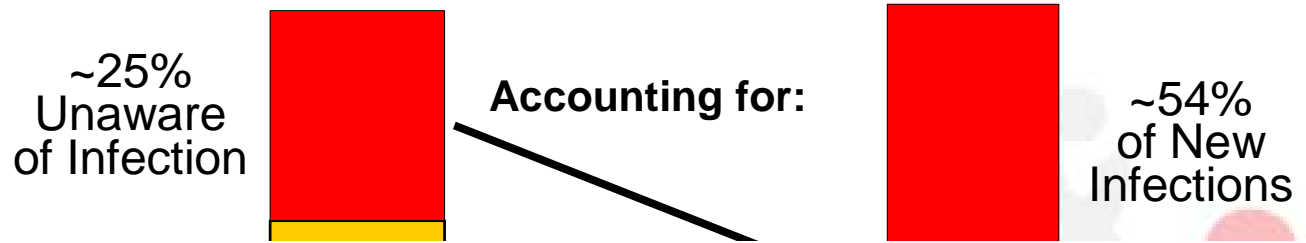
Awareness of serostatus among persons with HIV and estimates of transmission: US CDC&P estimates



Marks *et al.* AIDS 2006 26



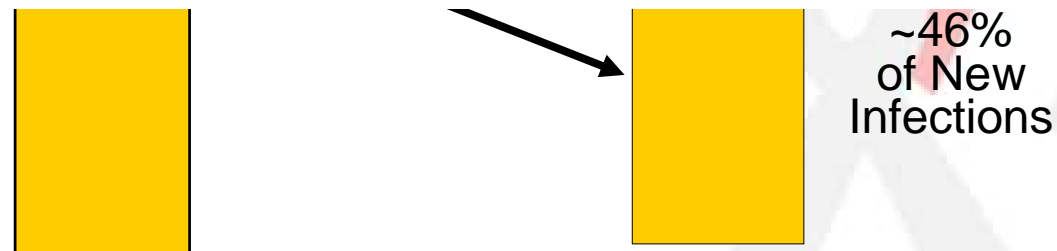
Awareness of serostatus among persons with HIV and estimates of transmission: US CDC&P estimates



the transmission rate from the unaware group was 3.5 times that of the aware group

Ar
lr

after adjusting for population size differences between groups



People Living with HIV/AIDS:
1,039,000-1,185,000

New Sexual Infections Each
Year: ~32,000



Marks *et al.* AIDS 2006 20

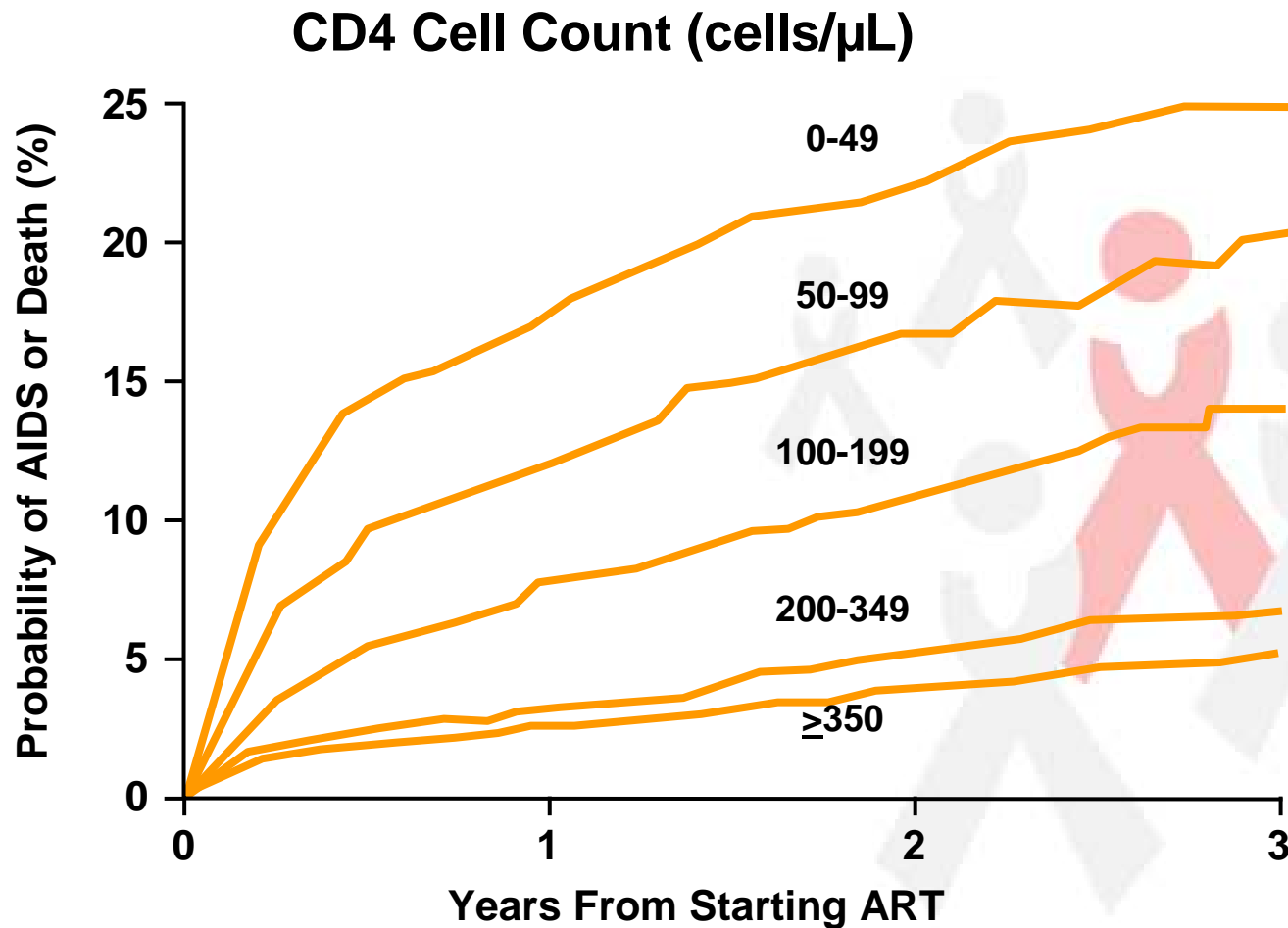


Classification of the patients according to baseline and last determination of CD4+ T cells after a median f/u 3 years

CD4+ T cells/mm ³ at baseline*	CD4+ T cells/mm ³ at last determination*				Total
	<200	200-349	350-499	>=500	
<200	91 (31)	94 (32)	62 (21)	48 (16)	295
200-349	15 (8.5)	28 (16)	39 (22)	94 (53.5)	176
350-499	2 (2)	4 (3)	21 (19)	85 (76)	112
>=500	0 (0)	2 (4)	5 (9)	47 (87)	54
Total	<i>108 (17)</i>	<i>128 (20)</i>	<i>127 (20)</i>	<i>274 (43)</i>	<i>637</i>

*Number of patients (%); García F, et al. J AIDS. 2004.

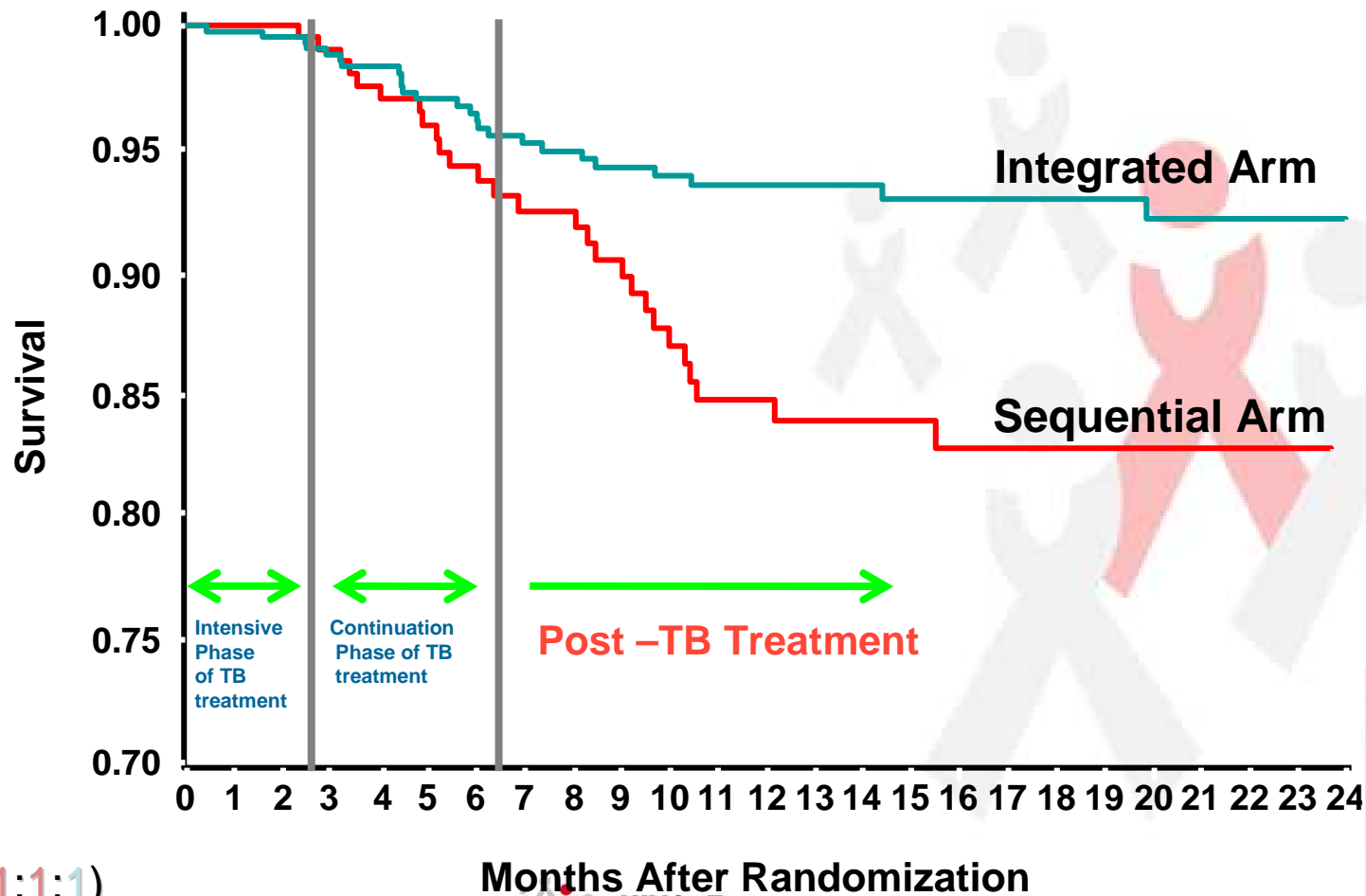
Prognosis from starting ART according to pre-therapy CD4 cell counts and HIV-RNA levels



ART CC. Egger et al, *Lancet*



Mortality for early (integrated with TB) versus deferred (**sequential**) start of ART (ddl, 3TC, EFV) in patients with active TB (SAPiT Trial)



N=642 (1:1:1)

HIV in Europe

Abdool Karim et al. 16th CROI; 2



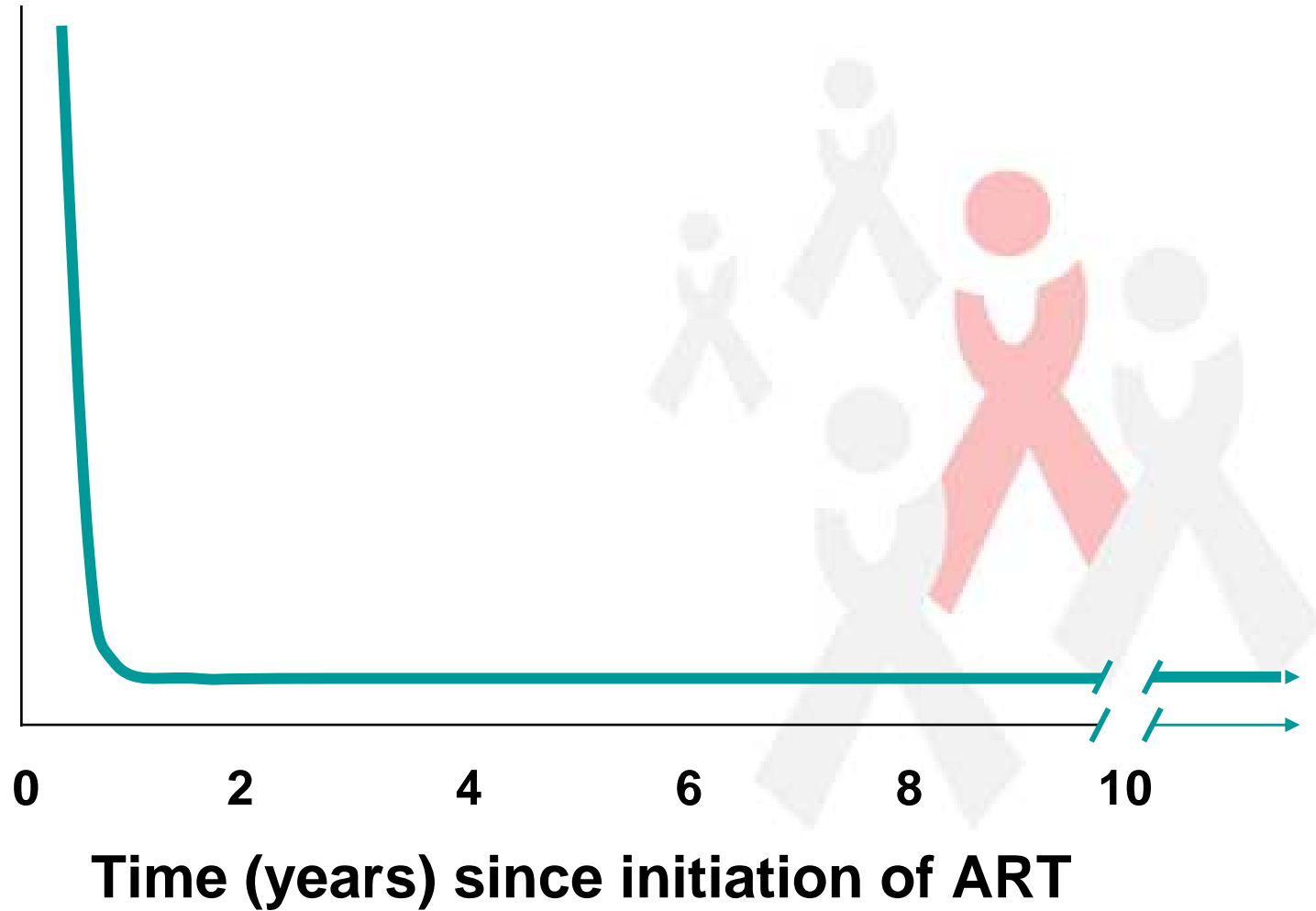
When to start antiretroviral therapy (ART) in adults ? – Summary of current guidelines

Guidelines	symptoms or CD4 <200	CD4 350-500	CD4 >500
EACS, : www.eacs.eu	treat	treat →	consider treat
DHHS, : www.aidsinfo.nih.gov	treat	treat →	Treat

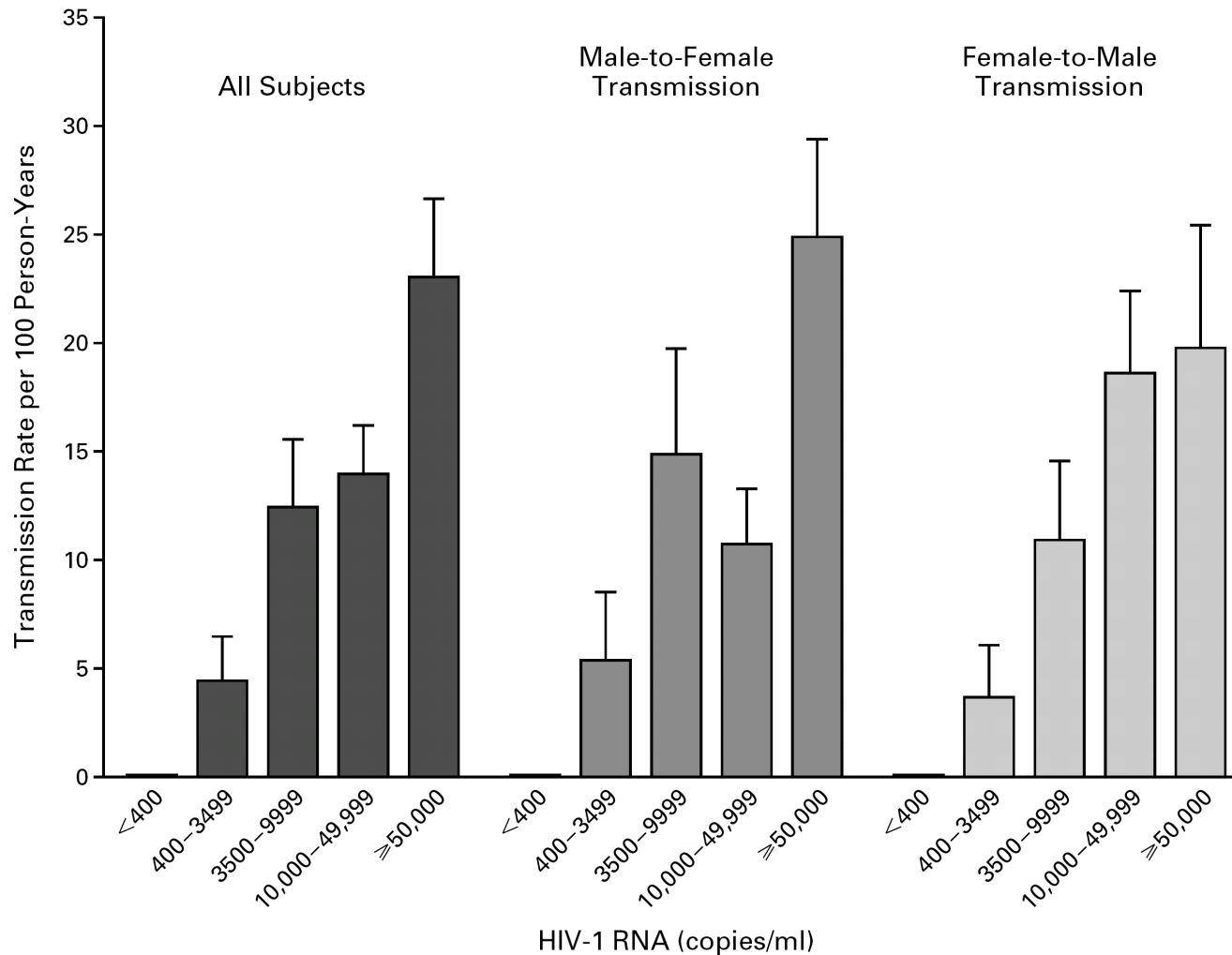


Aim of ART while using ART

HIV-RNA (copies/mL) in blood



Heterosexual transmission risk



N=415
(50 for
HIV-RNA
<400)

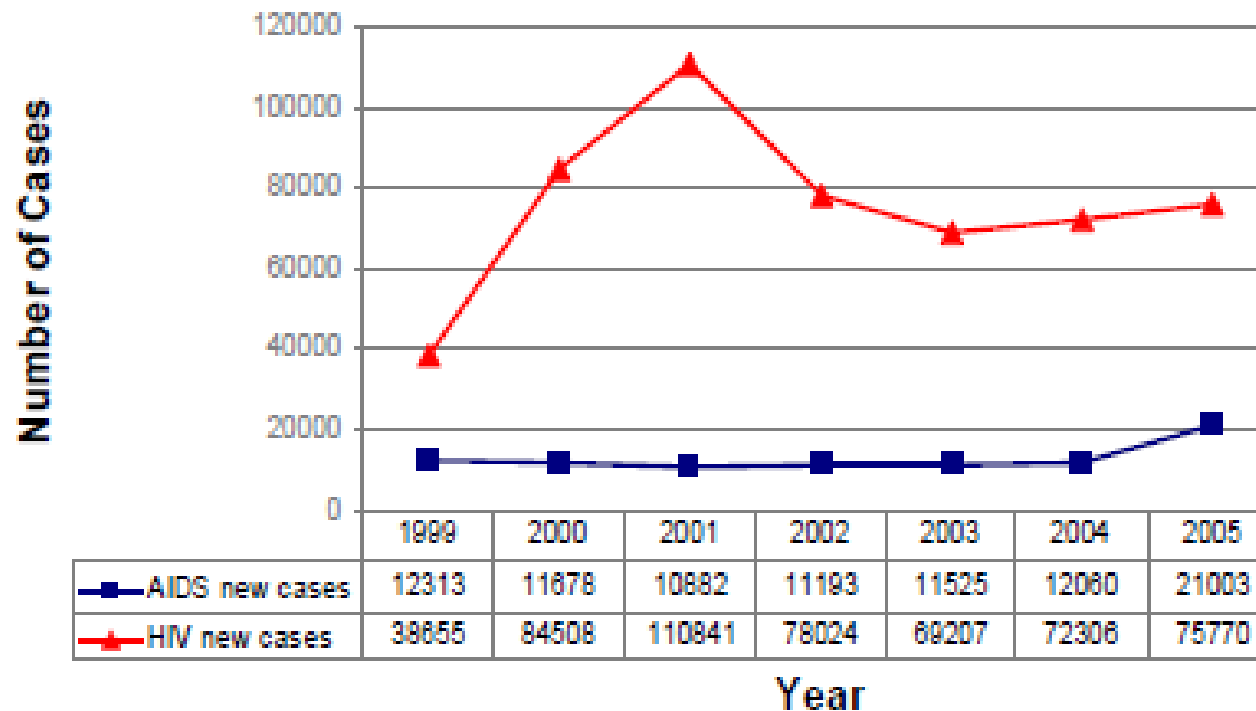


Quinn *et al*,



But ART has not improved overall European control of the epidemic

European countries: AIDS and HIV Incidences



Source: EuroHIV, Incl. EU27, N, CH, Belarus, Moldavia, Russian Federation, Ukraine



Early diagnosis of HIV infection



Terminology

- **Universal vs. Indicator (focused) testing**

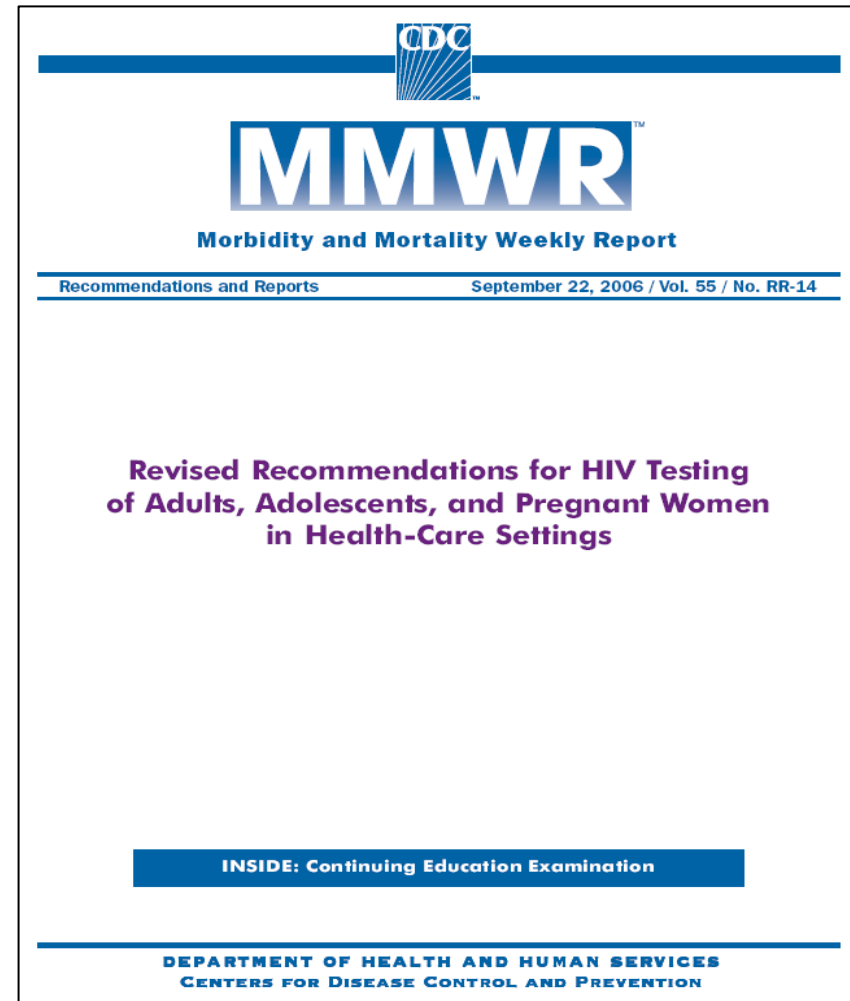
(every body 15-60 yrs. vs. Detection of an indicator disease/situation)

- **Opt out vs. Opt in**

(yes except explicit rejection vs. no except explicit permission)

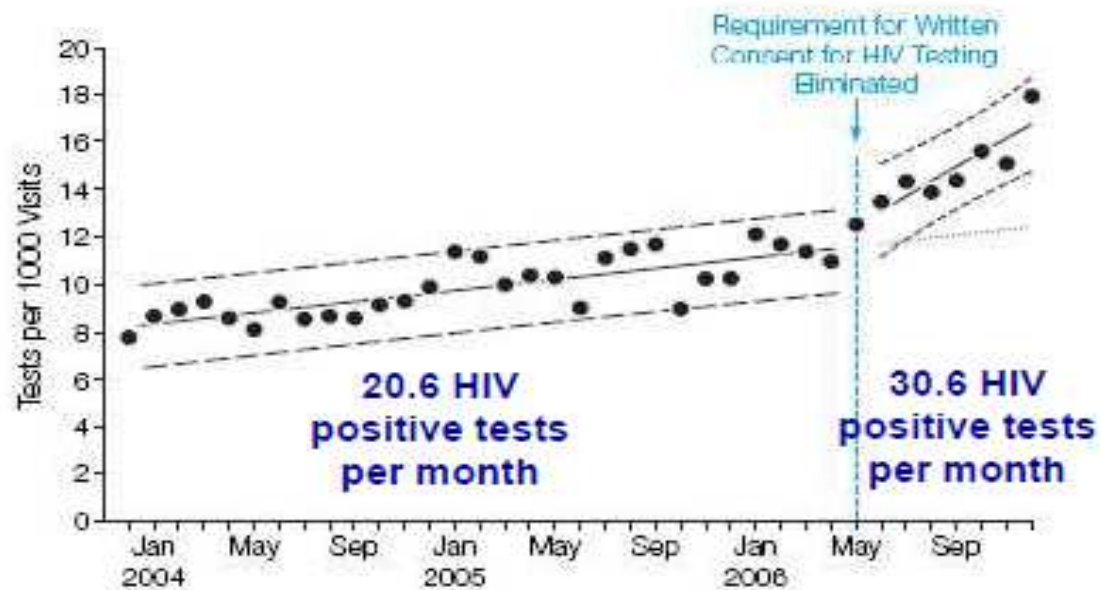
CDC Recommendations for HIV Testing in Healthcare Settings

- ▶ Routine voluntary testing for patients ages 13 to 64 years in healthcare settings
 - Not based on patient risk
- ▶ Opt-out testing
 - No separate consent for HIV
 - Resulting in increases in HIV testing rates
- ▶ Pretest counseling not required
- ▶ Repeat HIV testing left to discretion of provider, based on risk
- ▶ Within the US, 34 states are neutral to supportive of the CDC guidelines while 11 states have taken steps to reduce regulatory barriers
 - 6 states passed legislation (2007)



ESTRATEGIA OPT-OUT

San Francisco

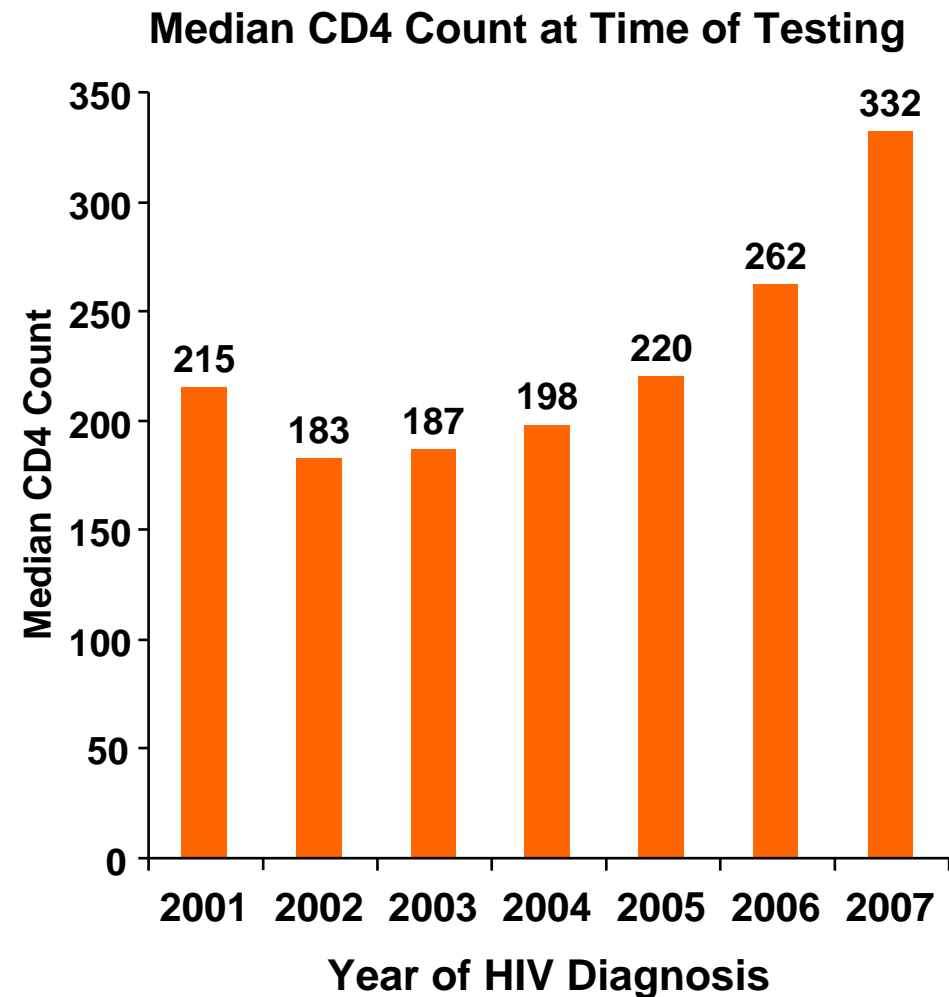


Zetola et al, JAMA March, 2007

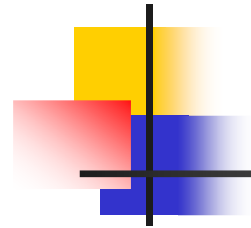


Washington DC HIV Testing Expansion: Earlier Diagnosis Helps Identify HIV+ People at Higher CD4+ Counts

- ▶ Expanding HIV testing in jails, schools, needle exchange, and couples services
- ▶ Through these efforts they were able to increase the number of tests given from 43,271 tests done in 2007 to 72,864 tests done in 2008 (68.4% increase)
- ▶ In addition, they were able to find patients with higher CD4 counts at initial testing
 - 2004 – 198 cells/mm³
 - 2007 – 332 cells/mm³



Early diagnosis of HIV infection



- Indicator (focused) testing (Opt in)

All AIDS indicator diseases

Pregnant women

Donors (blood, organs etc.)

All diseases/situations where prevalence
of HIV infection
suspected/confirmed above
0.1-1%

HIV Screening by Potential AIDS Defining Event in a Privately Insured US Population

Review of 8 US Health Plans - 7,451 patients

Potential AIDS Defining Event	N	Screening Rate
Burkitt's or immunoblastic lymphoma or primary lymphoma of brain	2,980	3.0%
Encephalopathy	2,066	5.0%
Invasive cervical cancer	958	4.4%
Candidiasis of bronchi, trachea, lung, or esophagus	542	7.0%
Histoplasmosis, disseminated or extrapulmonary	370	2.2%
Wasting /Cachexia	350	4.3%
Disseminated herpes or herpes meningitis	94	13.8%
<i>M. avium</i> or <i>M. kansasii</i> , disseminated or extrapulmonary	67	13.4%
<i>Pneumocystis carinii</i> pneumonia	48	10.4%
Kaposi's sarcoma	35	8.6%
Progressive multifocal leukoencephalopathy	20	0.0%
CMV pneumonia or retinitis	16	25.0%
Coccidioidomycosis, disseminated or extrapulmonary	13	7.7%
Cryptococcosis, extrapulmonary	11	9.1%
Misc (toxoplasmosis of brain, chronic isosporiasis, salmonella septicemia, chronic cryptosporidosis)	5	20.0%

- ▶ **4.3% Patients Screened for HIV with Any Potential AIDS Defining Event**
- ▶ **12.5% Patients Screened for HIV with Multiple Potential AIDS Defining Events**

The HIV in Europe Indicator Diseases Project

Participation of countries

39 centres in 17 countries

1. Sexually transmitted diseases (24)
2. Malignant lymphoma, irrespective of type (8)
3. Cervical or anal dysplasia or cancer, (5)
4. **Herpes zoster in a person younger than 65 years (9)**
5. Hepatitis B or C virus infection (26)
6. **Ongoing mononucleosis-like illness (10)**
7. **Unexplained leukocytopenia or thrombocytopenia lasting at least 4 weeks (8)**
8. **Seborrheic dermatitis / exanthema (12)**



- **Conocer la situación basal de partida en nuestros CAP**
- **Estudio retrospectivo año 2008**

- **CAP, EI, edad, sexo, nacionalidad**
- **Presencia de factores de riesgo clásicos para VIH, antecedentes de enfermedades de transmisión sexual (ETS), hepatitis (VHB, VHC) o VIH**
- **Solicitud de serología para VIH**
- **Resultado de la serología VIH**



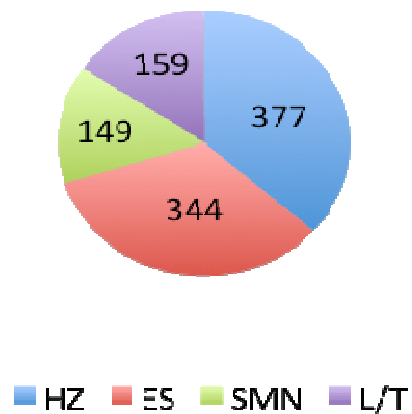
RESULTADOS

N = 1029 pacientes

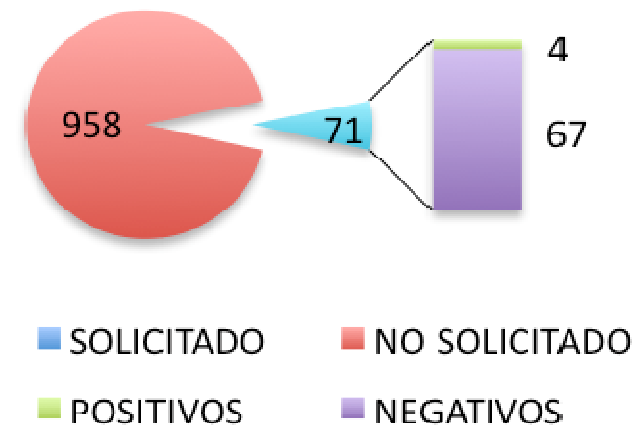
Edad media 51 años (15-95 años, DE 20)

56.4% mujeres, 1.3% homosexuales

ENFERMEDADES INDICADORAS (N)

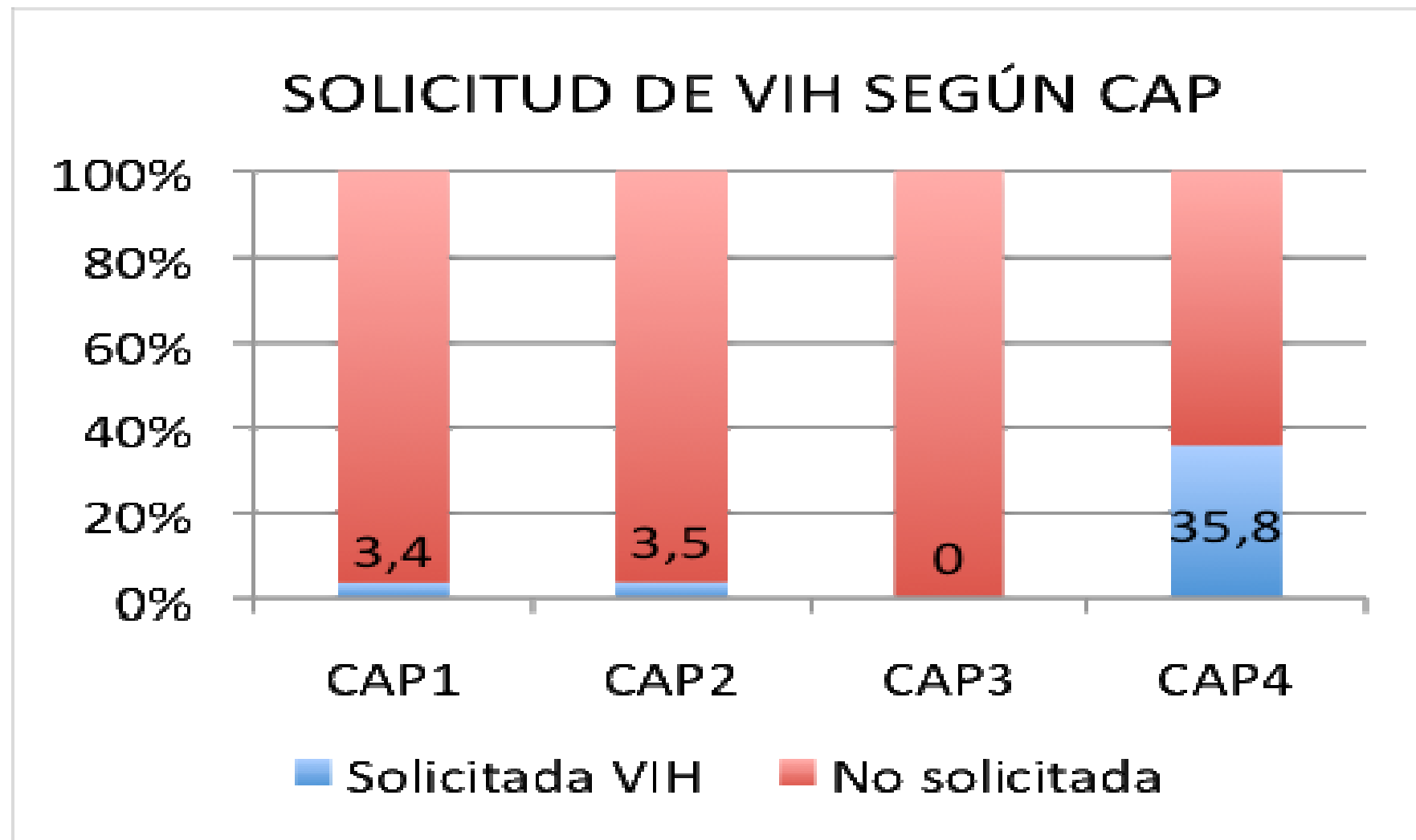


SOLICITADO VIH



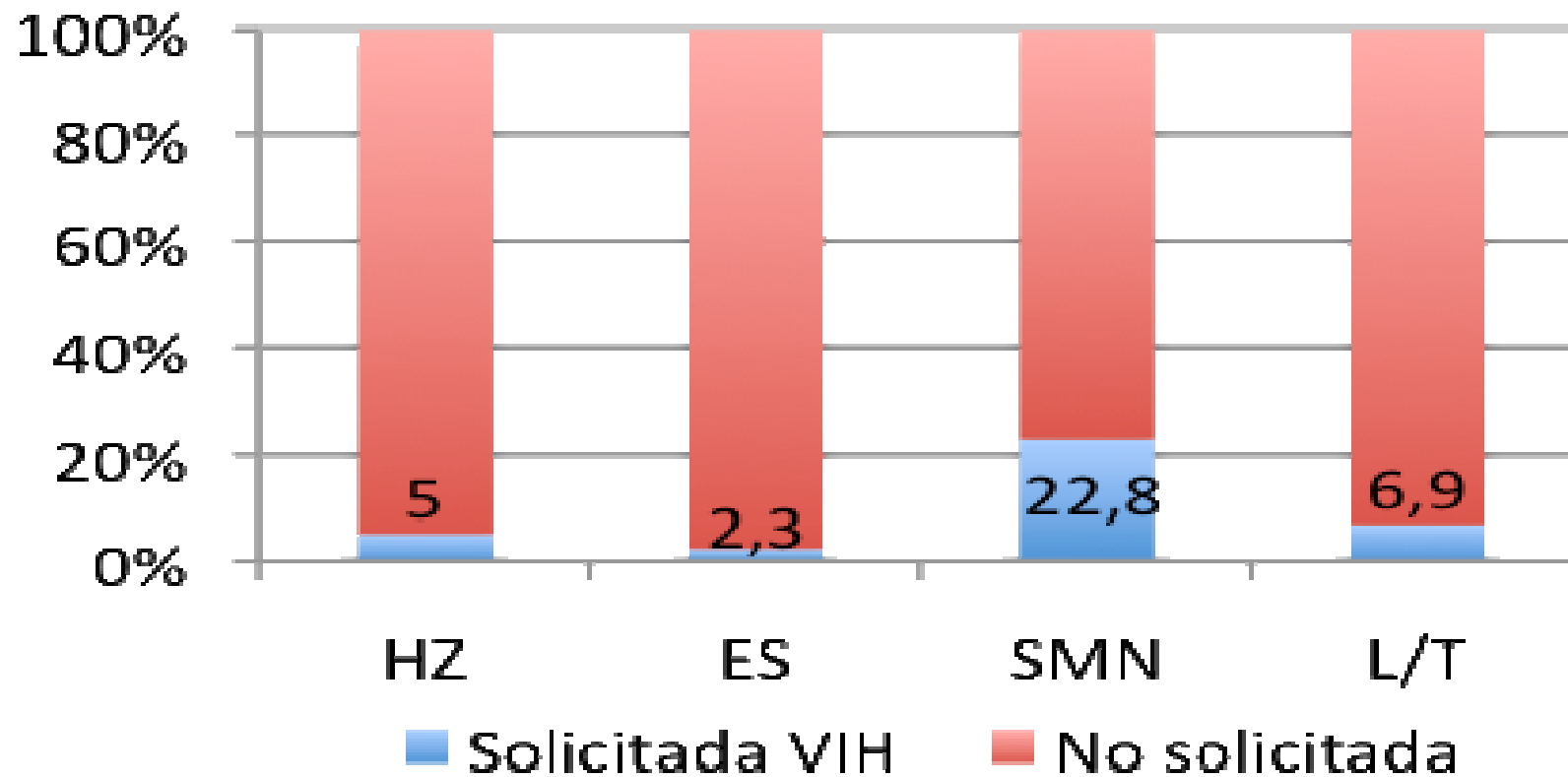
**Prevalencia:
5.6% (95%CI: 1.5-13.8)**

RESULTADOS



RESULTADOS

SOLICITUD DE VIH SEGÚN ENFERMEDAD INDICADORA



CONCLUSIONES

- **La búsqueda activa de infección por VIH en enfermedades indicadoras actualmente es extremadamente baja, incluso en pacientes que consultan por mononucleosis.**
- **La solicitud de VIH se basa más en criterios como el área de salud, la edad, género, nacionalidad y antecedentes de otras ETS.**

Indicator disease-guided testing for HIV – the next step for Europe?

B Gazzard,¹ N Clumeck,² A d'Arminio Monforte³ and JD Lundgren⁴ *HIV Medicine* (2008), 9 (Suppl. 2), 34–40

While the CDC's recommendations have been widely accepted by clinicians in the US, even if they have expressed concern about the lack of additional resources for treatment, the policy may not be appropriate for HIV testing in Europe. This is because the health system in Europe varies considerably from that in the US. Although access to care is free at the point of delivery in most countries, limited availability of HIV care and stigma associated with the disease remain widespread. Consequently, universal HIV testing may not be acceptable to most European governments at the present time.

DIAGNOSTICO PRECOZ EN 4 CAP EN BARCELONA: ESTUDIO PROSPECTIVO

- **Estrategia Opt out: ofrecerlo a todos los pacientes entre 18-65 años que acudan a los CAPs**
- **Estrategia Opt in: ofrecerlo a aquellos pacientes entre 18-65 años que acuden por 4 enfermedades indicadoras:**
 - **Herpes Zóster**
 - **Síndrome mononucleósico**
 - **Leucopenia/trombopenia**
 - **Eccema seborreico**

Objectives

In primary care centers:

1. To test all persons with 4 selected indicator conditions (Indicator strategy).

2. To test in a randomly selected sample (1/10) the remaining patients attending these centers (Universal strategy).

Methods

- A multicenter, prospective study in 4 Primary Care Centers (PCC) of Barcelona was undertaken (September 2009-March 2011)
- Eligible patients: 18-65 years old.

Indicator strategy	Universal strategy
Herpes Zoster Seborrheic Eczema Mononucleosis S Leucopenia/Thrombopenia >4 weeks	1 of every 10 randomly selected patients visited for other than the previous indicator conditions.

Methods

- Written inform consent.
- Questionnaires: Sociodemographic and sexual behavior; HIV testing history and clinical information.
- Patients recruited in indicator strategy were included in HIDES I of HIV in Europe.
- Blood rapid test (Determine® HIV-1/2 Ag/ Ab Combo)
Cost for 1 test: 6€.
- Education and training of staff involved

Results

Indicator strategy	Universal Strategy
Primary Care census with the 4 selected indicators 775 Offered screening* 89 Accepted screening 85 Completed testing 85	Primary Care census 66043 Offered screening (random selection 1/10)* 344 Accepted screening 313 Completed testing 304

*Only committed participating physicians during selected periods of the week

Indicator strategy		Universal Strategy	
Census	Offer rate	Census	Offer rate
775	11.5 %	66043	0.5%
Offered screening	Acceptance R	Offered screening	Acceptance R
89	94.4%	344	90.9%
Accepted Scre.	Completion R	Accepted Scre.	Completion R
85	100%	313	97.1%
Completed testing	Overall rate	Completed testing	Overall rate
85	10.9%	304	0.46%

Comparison baseline characteristics

Variable	Indicator	Universal	P
Age*	36 (30-50)	35 (28-49)	0,85
Male**	60 (71)	117 (39)	0,0001
PCC**			
C1, C2, C3	38 (45)	261 (86)	0,0001
C4	47 (55)	42 (14)	
MSM*	8 (9)	16 (5)	0,27
Never used Condoms *	42 (49)	128 (42)	0,002
Previous STD	12 (14)	19 (6)	0,021
N° 3-5 Visits HCS	6 (7)	1 (0.3)	0,0001
Previous HIV test	29 (34)	123 (41)	0,12

*: Number (%). **:Median (IQR).

HIV prevalence

Indicator strategy	Universal strategy
<p data-bbox="322 671 1048 746">Completed testing: 85</p> <p data-bbox="439 887 931 954">HIV Positive: 4</p> <p data-bbox="488 1107 882 1174">Prevalence</p> <p data-bbox="293 1209 1077 1284">4.7% (95%CI: 1.3-11.6)</p>	<p data-bbox="1189 671 1957 746">Completed testing: 304</p> <p data-bbox="1323 887 1805 954">HIV Positive: 1</p> <p data-bbox="1373 1107 1767 1174">Prevalence</p> <p data-bbox="1155 1209 1984 1284">0.3% (95%CI: 0.01-1.82)</p>

P= 0.009

Baseline characteristics of HIV newly diagnosed

Variable	Indicator n=4	Universal n=1
Male	4	1
Median Age	38	32
PCC	C4	C2
Caucasian	3	1
MSM	3	1
1-3 Visits to HCS	4	1
Actual ID		
MNS	2	Dermatitis
L/T	2	
≥4 sexual partners/year	3	1
Previous STD	3	1
Previous HIV test	3	1

Direct cost per new HIV diagnosis

Indicator strategy	Universal strategy
<p>HIV Prevalence 4.7% (95%CI: 1.3-11.6) Primary Care census 775</p> <p>Potential HIV + 36 (95%CI: 25-49)</p> <p>Overall Cost 4,650 euros Cost per HIV diagnosis 129€ (95%CI: 107-153)</p>	<p>HIV Prevalence 0.3% (95%CI: 0.01-1.82) Primary Care census 66043</p> <p>Potential HIV + 198 (95%CI: 171-227)</p> <p>Overall Cost 396,258 euros Cost per HIV diagnosis 2,001€ (95%CI: 1,913-2,088)</p>

Discussion: Comparison with HIDES I

Indicator strategy

HIV Prevalence

4.7% (95%CI: 1.3-11.6)

HIDES I MON+CYT combined (n=535)

3.7% (95%CI: 2.3-5.7)

Potential HIV +

28 (95%CI: 18-40)

Direct Cost per HIV diagnosis

166€ (95%CI: 141-193)

CONCLUSIONES

- **La estrategia opt out** es una estrategia muy adecuada, pero puede tener problemas de implementación:
 - Legales, autorización del paciente,..
 - Preparación del personal que hace la prueba
 - Recursos
- **La estrategia opt in** tiene una serie de ventajas:
 - No tiene problemas legales, la indicación es clínica
 - Los recursos necesarios son menores
 - Detecta casos precoces si se escogen todas las enfermedades indicadoras con prevalencia entre 0.1-1%
 - Es potencialmente capaz de detectar a un número de pacientes no muy inferior al de la estrategia opt out

CONCLUSIONES

- **CUALQUIER ESTRATEGIA QUE MEJORE LA DETECCIÓN PRECOZ ES INELUDIBLE EN LOS PROXIMOS AÑOS**
- Grupo de Atención Primaria y Hospitalaria para la detección precoz del VIH:
 - Natalia López¹, Mercè Muns², Zoe Herreras³, Ethel Sequeira⁴, Pilar Navarrete³, Ignacio Pérez⁶, Thaïs Clusa², Mercedes Poveda⁴, Luisa Benito¹, Josep Maria Vilaseca³, Marta Catalán⁴, Antoni Sisó¹, Joan Caylà⁵, Patricia García de Olaya⁵, Emma Fernández⁶, Anna Pereira³, Laura Sebastián¹, Ágata León⁶, Felipe García⁶, José María Gatell⁶
 - ¹CAP LES CORTS (GesClínic), ²CAP RAVAL SUD, ³CAPSE ROSELLÓN, ⁴CAPSE CASANOVA, ⁵Agencia de Salud Pública de Barcelona, ⁶Servicio de Infecciones del HOSPITAL CLINIC
- Nuchi Sánchez: UTSI CAPSE-GesClínic
- Anna Vilalta y Minerva Mas, CAP Les Corts