

I Congreso de GESIDA – Madrid, 21-24 de Octubre del 2009.

Supervivencia a 5 años de Pacientes Coinfectados por VHC-VIH Trasplantados Hepáticos: un Estudio de Casos y Controles

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HIV cohort (1983-2009)

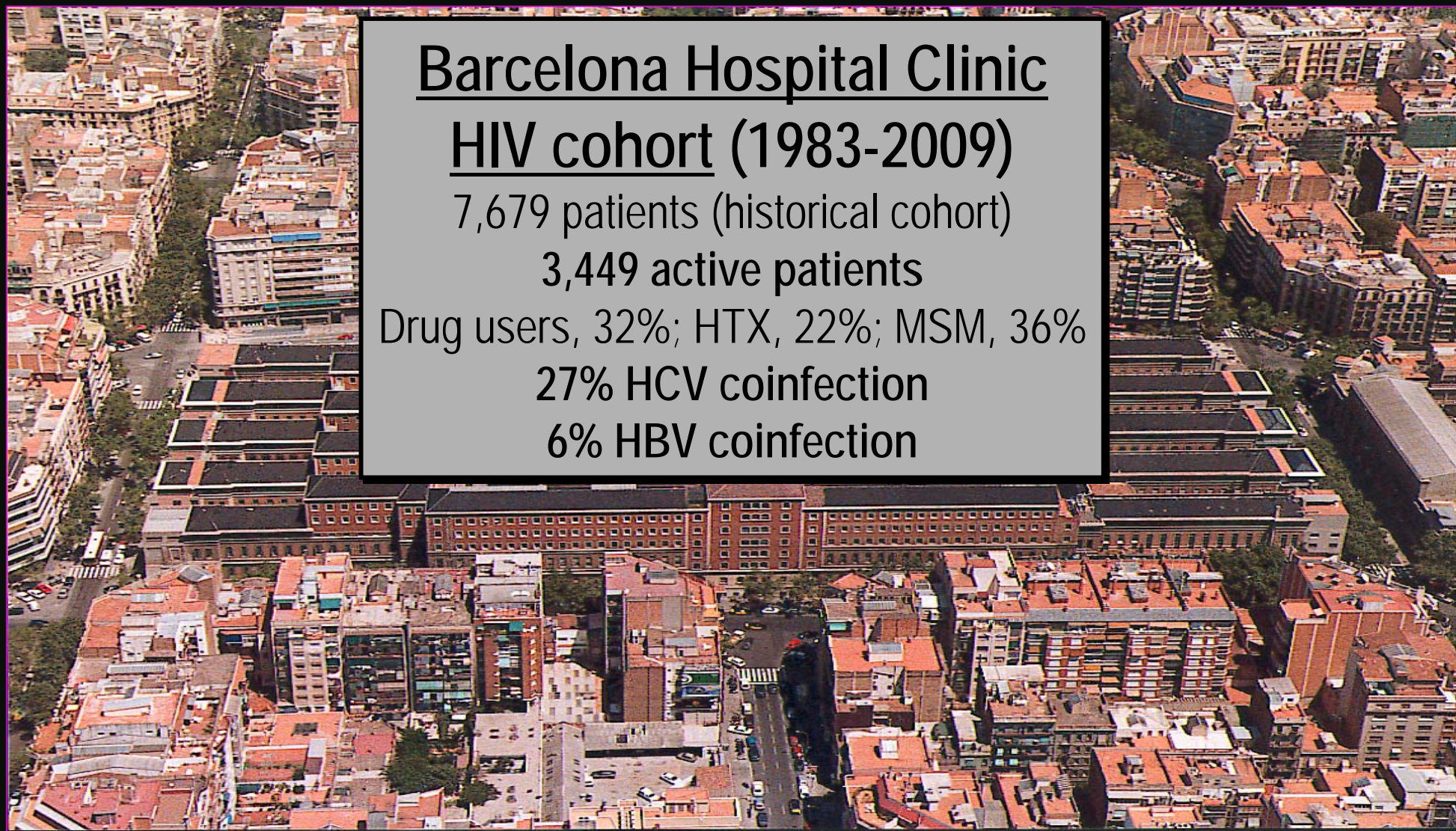
7,679 patients (historical cohort)

3,449 active patients

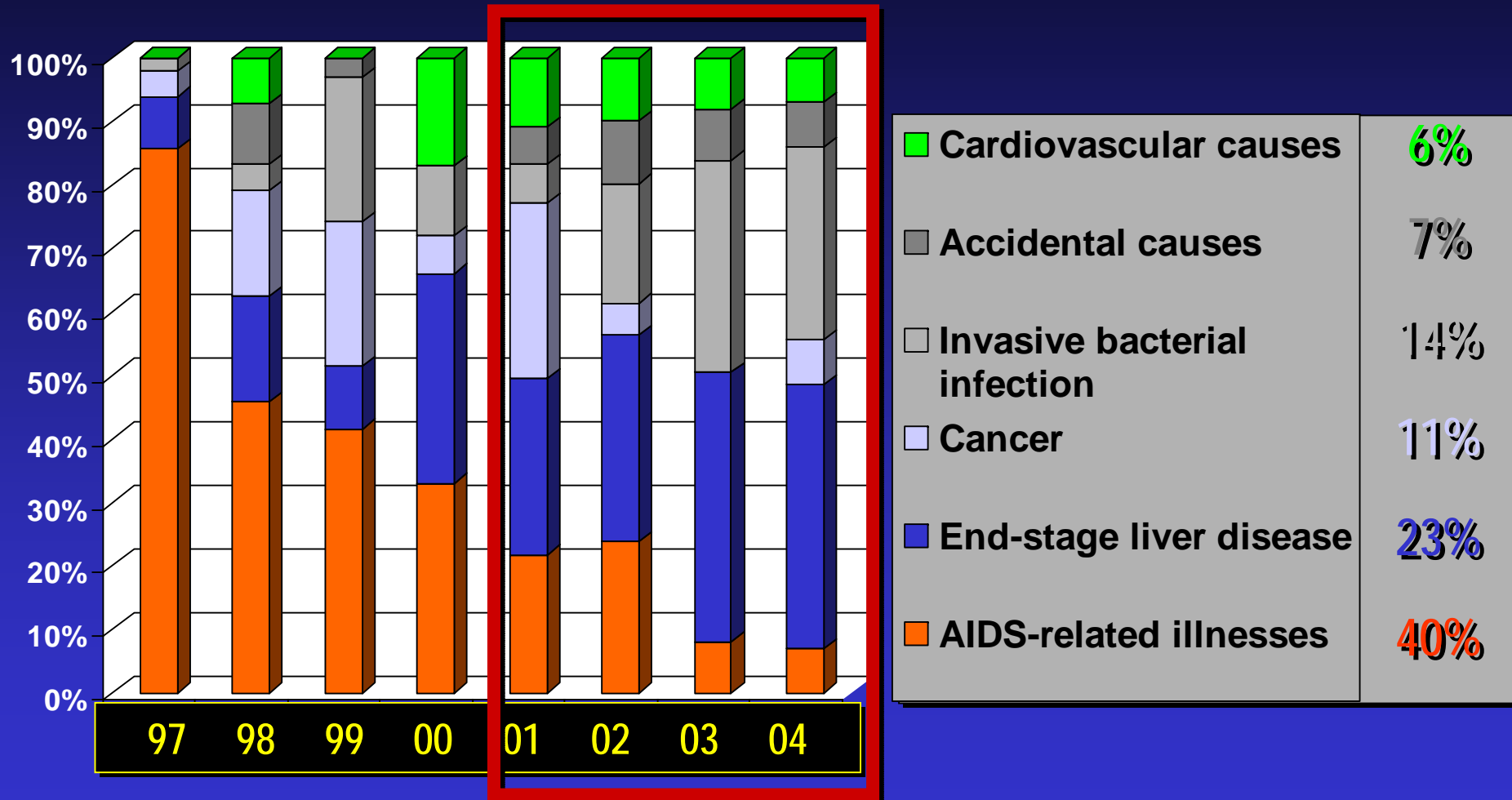
Drug users, 32%; HTX, 22%; MSM, 36%

27% HCV coinfection

6% HBV coinfection



Causes of Death in 235 HIV-1-Infected Patients Barcelona Hospital Clinic HIV Cohort (1997-2004)



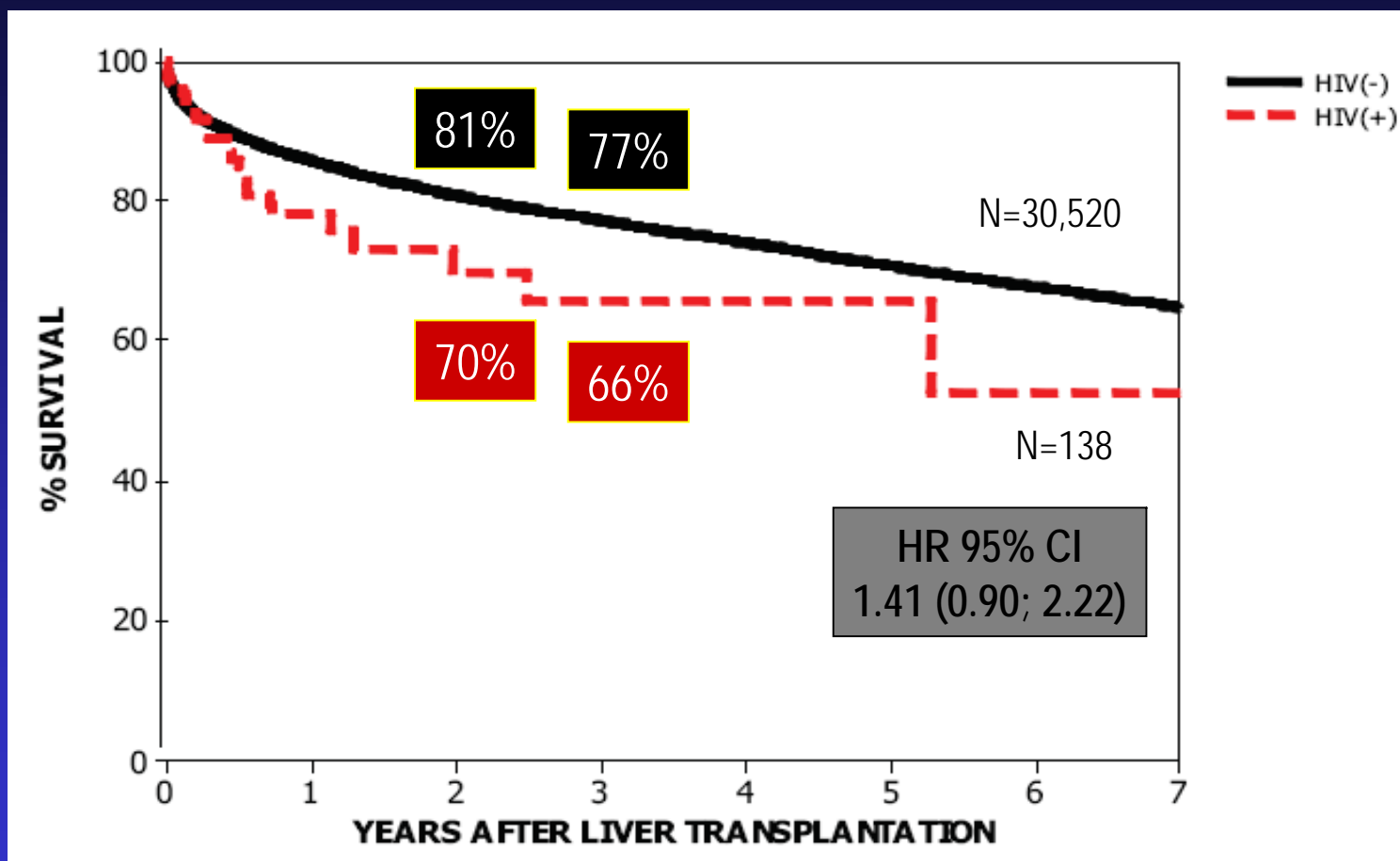
Martinez E. et al. HIV Medicine. 2007; 8: 251-258.

Countries Performing Liver Transplants in HIV-Infected Patients

- U.S.A (No. \approx 160)
- Spain (No. \approx 190)
- France (No. \approx 120)
- Italy (No. \approx 80)
- U.K. (No. \approx 40)
- Germany (No. \approx 30)
- Switzerland (No. \approx 10)
- Other countries

Impact of HIV on Survival After OLT: Analysis of United Network for Organ Sharing Database (1997-2006)

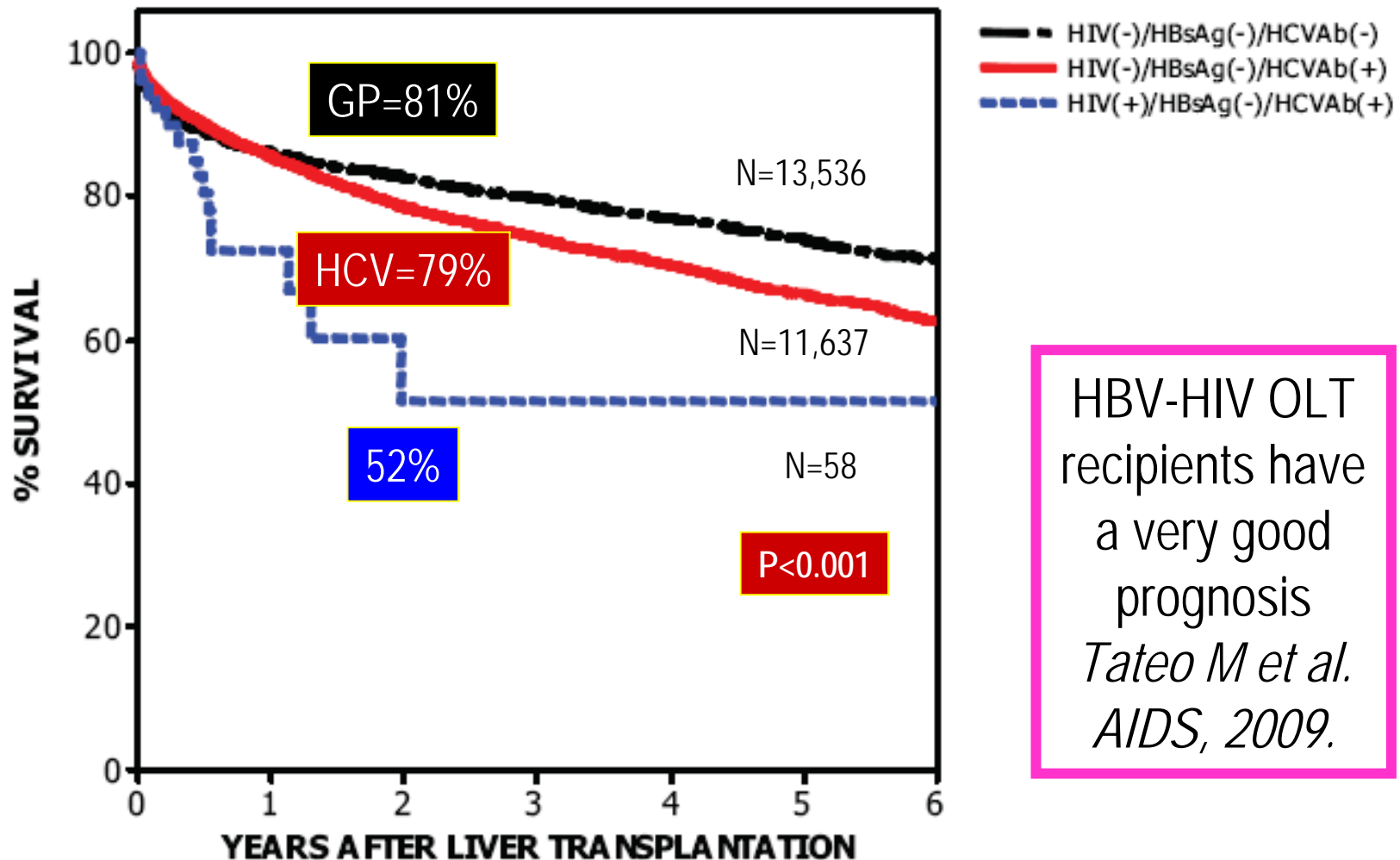
Mindikoglu AS et al. Transplantation 2008;85: 359–368.



The 24 HIV-infected patients who did not have HBV or HCV were alive after an average of 1.2 years of follow-up per person.

Impact of HIV on Survival After OLT: Analysis of United Network for Organ Sharing Database (1997-2006)

Mindikoglu AS et al. Transplantation 2008;85: 359–368.



BACKGROUND

Preliminary studies performed in single centers with small numbers of OLT recipients suggest poorer survival in HCV/HIV-coinfected than in HCV-monoinfected patients. Prognostic factors of mortality are not well known.

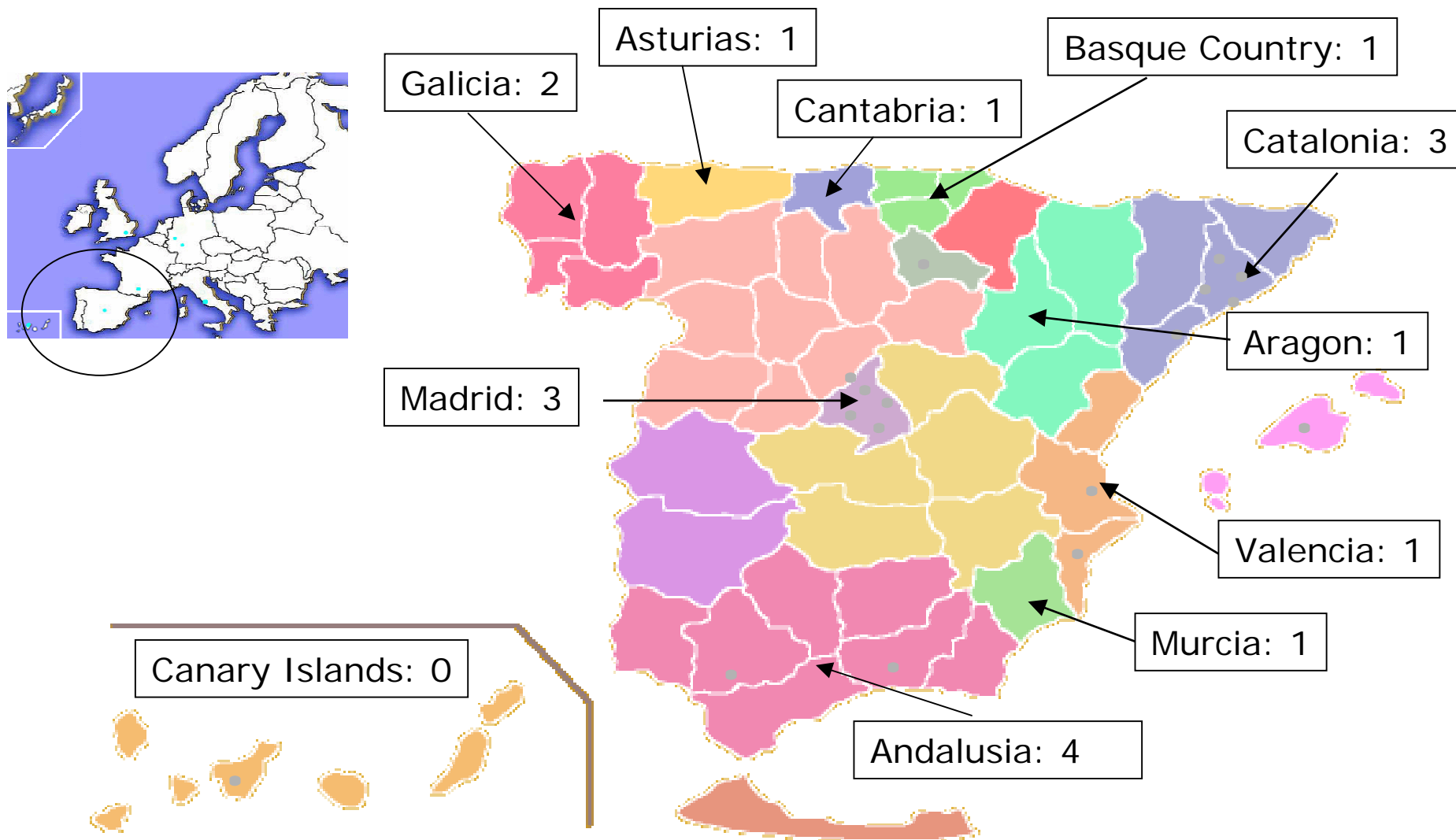
OBJECTIVE

To study 5-year survival in Spanish HCV/HIV-coinfected and HCV-monoinfected OLT recipients and to know the prognostic factors of mortality in HCV/HIV-coinfected OLT recipients.

PATIENTS & METHODS

- Prospective study of the first 84 HCV/HIV-1–infected patients who underwent OLT in Spain (2002-06).
- Variables analyzed:
 - **Pre-OLT recipient variables:** HIV (stage, CD4 cell count, plasma HIV-1 RNA viral load, cART regimens) and liver disease (MELD, Child, plasma HCV RNA viral load)
 - **Donor and operative variables**
 - **Post-OLT variables:** immunosuppression, rejection, infection, toxicity and the HIV variables described above.
- HIV-infected recipients were administered the same immunosuppression and prophylaxis as HIV-negative patients.

Geographic Distribution of the 18 Hospitals Participating in the OLT-HIV FIPSE/GESIDA Cohort Study (2002-11)



ACCEPTANCE CRITERIA FOR OLT*

- **Liver criteria:** the same as for the non-HIV-infected population.
- **HIV criteria:**
 - 1) **Clinical:** no previous C events (CDC, 1993) except some OIs (TB, Can, PCP); and,
 - 2) **Immunological:** pre-OLT CD4 cell count >100 cells/mm³ for OLT; and,
 - 3) **Virological:** HIV-1 RNA viral load BDL on cART or, if detectable, post-SOT suppression predicted.
- **Drug abuse criteria:** A) No heroin or cocaine abuse for >2 years; B) No alcohol abuse for >6 months.

* Miró JM et al. Enferm Infecc Microbiol Clin. 2005; 23:353-362.

CASES AND CONTROLS (1:3 ratio)

- **Cases (HCV/HIV-coinfected patients)**
 - **84 consecutive HCV/HIV-coinfected** patients with OLT between 2002 and 2006 and followed until 2008.
 - Data were obtained from the FIPSE OLT-HIV-05-GESIDA 45-05 database.
- **Controls (HCV-monoinfected patients)**
 - HIV-infected recipients were matched with **252 HCV-monoinfected** patients who underwent OLT.
 - **Matching criteria:** site, age (± 12 years), gender, calendar year (± 1 year), HBV coinfection, and presence of hepatocellular carcinoma.
 - Data for HIV-negative recipients were obtained from the SETH database.

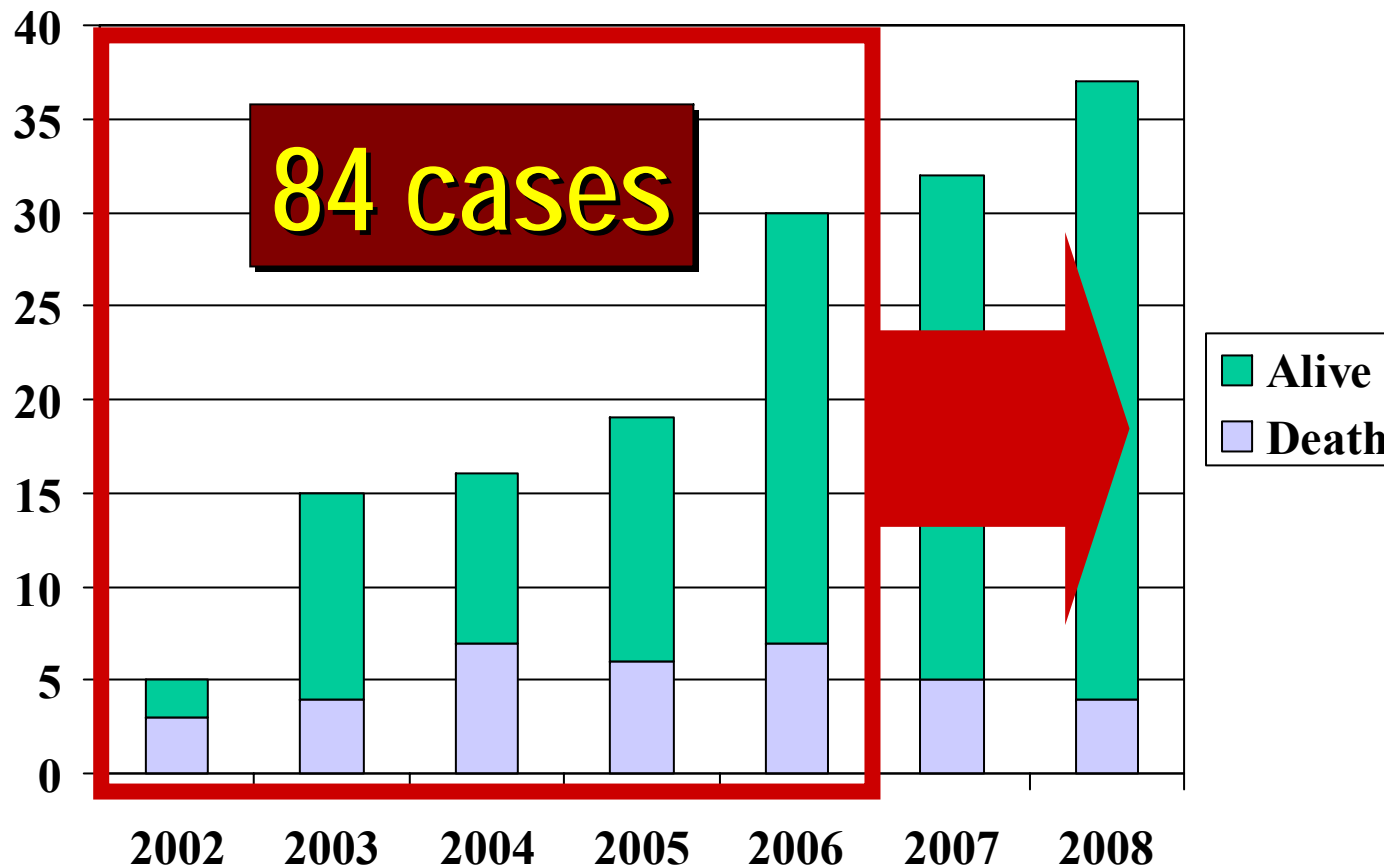
Limitations of the Control Group (N=252)

- ONT/SETH registry did not have the following information: **HCV genotype & viral load, MELD, anti-HCV Rx (SVR) and blood transfusion requirements during surgery**. In addition, the registry has **donor age and donor cause of death**.
- We collected these data retrospectively between March 2009 and July 2009.

STATISTICAL ANALYSIS

- Continuous variables were assessed using the *t* test for normally distributed data or the Mann-Whitney U test otherwise, and the Fisher exact test for categorical data.
- The Cox model was used to analyze the time to death, and all covariates with a $P < 0.10$ on univariate analysis were used to identify independent predictors of mortality.
- Patient survival analysis was performed using the Kaplan-Meier method, and groups were compared using the log-rank test and Cox regression analysis.
- The analysis was performed using SAS version 9.1.3 software (SAS Institute, Cary, NC, USA) and the level of significance was established at 0.05 (two-sided).

OLT in Spanish HIV-Infected Patients in the HAART Era (2002-09) (N=191)



Main Characteristics & Outcome (Feb, 2009)

	HIV+HCV N=84	HCV N=252
Male gender	78%	78%
Age (years)*	42	46
HBV coinfection	16%	16%
HCC**	8%	8%
Follow-up (yrs)*	2.6	1.9
Retransplantation	4 (5%)	12 (5%)
Death	30 (36%)	50 (20%)

* Median; ** Hepatocellular carcinoma.

Matched Characteristics and Outcome

	HIV+HCV N=84	HCV N=252
Male gender	78%	78%
Age (years)*	42	46
HBV coinfection	16%	16%
HCC**	8%	8%
Follow-up (yrs)*	2.7	3.4
Retransplantation	4 (5%)	17 (7%)
Death	33 (39%)	69 (27%)

* Median; ** Hepatocellular carcinoma.

Donor and Recipient Characteristics

HIV+HCV
N=84

HCV
N=252

Donor

- Age >60 years
- Gender (males)

37%

57%

29%

66%

Recipient

- Pre-OLT MELD score
- HCV Genotype 1/4
- SVR

15

69%

19%

15

75%

23%

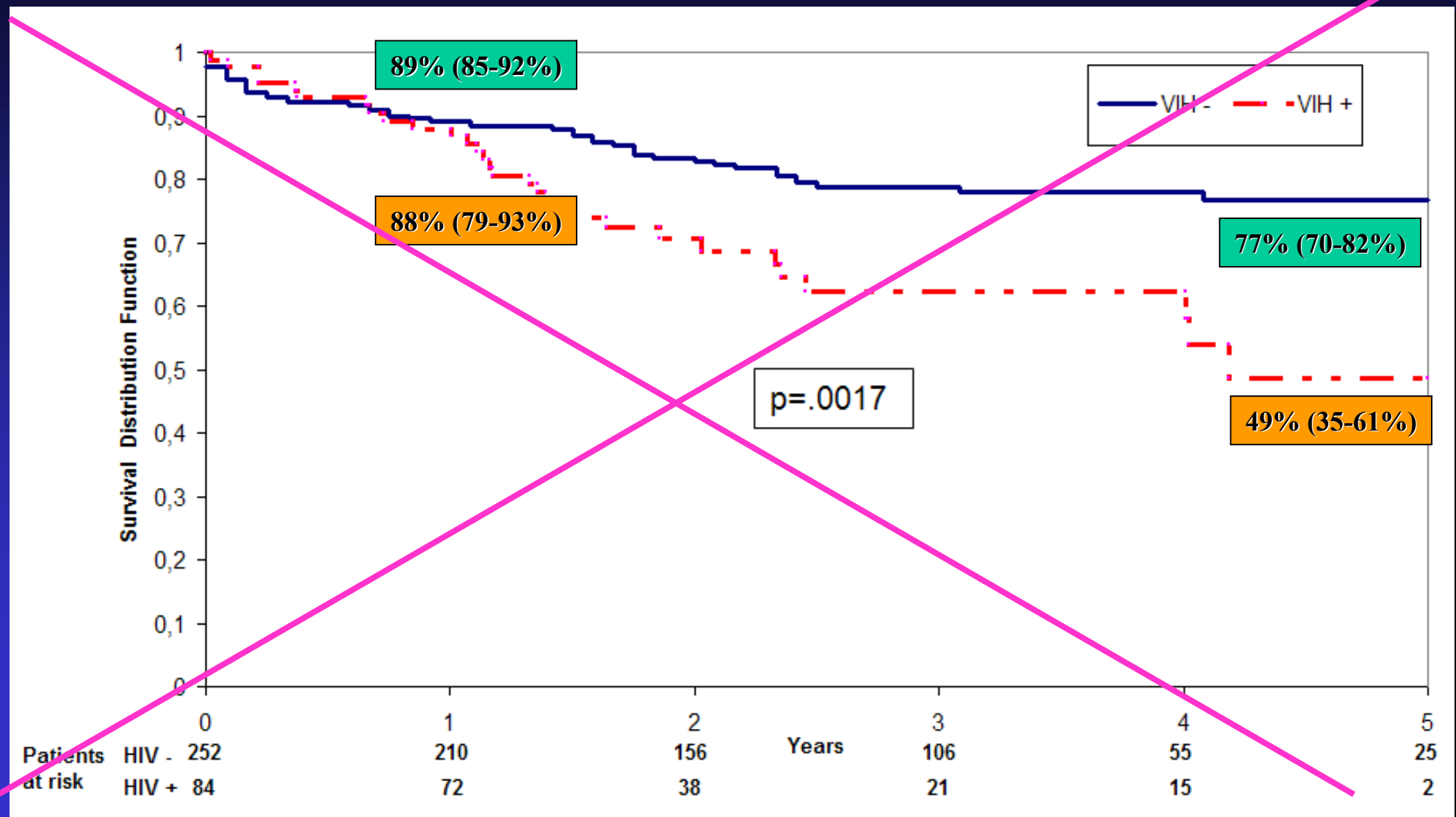
SVR = Sustained virological response.

Causes of Death in HIV+ and HIV- Recipients

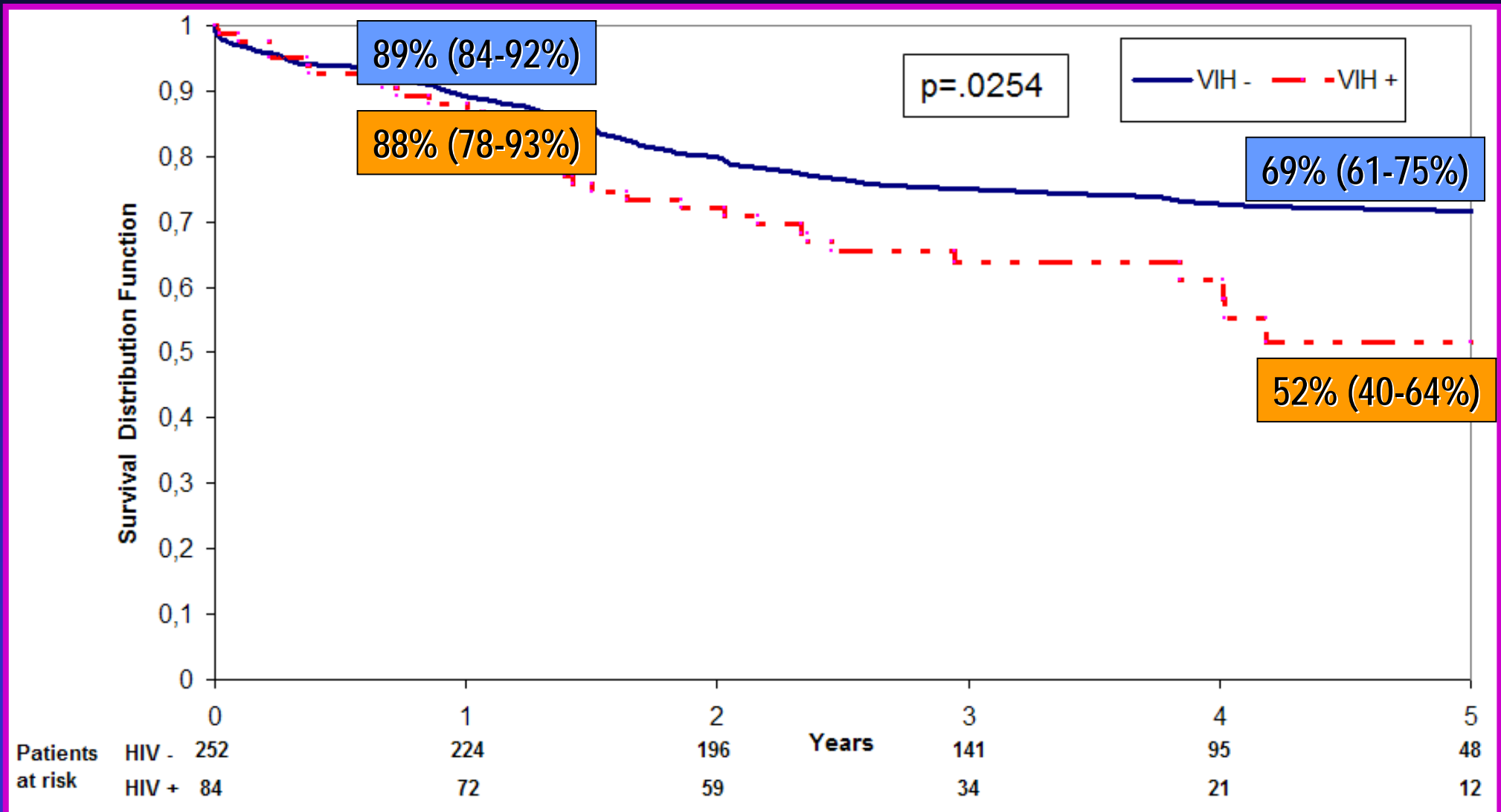
	HIV+HCV N=33	HCV N=69
Infections	20%	18%
HCV recurrence	47%	42%
Cancer	7%	4%
Technical complications	(-)	8%
Other	33%	28%

* Two patients had a recurrence of HCV and an infection as cause of death.

Case (N=84) - Control (N=252) Study: Patient Survival After OLT in HCV-Infected Patients According to HIV Status (Old)



Case (N=84) - Control (N=252) Study: Survival After OLT in HCV-Infected Patients According to HIV Status



Multivariate Analysis of Mortality

Donor and Recipient Pre-OLT Variables

Variable	HR (95% CI)	P value
MELD score		
- Pre-OLT (1 unit increase)	1.10 (1.03; 7.69)	.002
No. of OLT per Site		
- > 5 transplants	1	
- ≤ 5 transplants	4.54 (2.00;10.3)	<.001
Donor age		
- < 60 years	1	
- ≥ 60 years	2.16 (1.04;4.;49)	.04

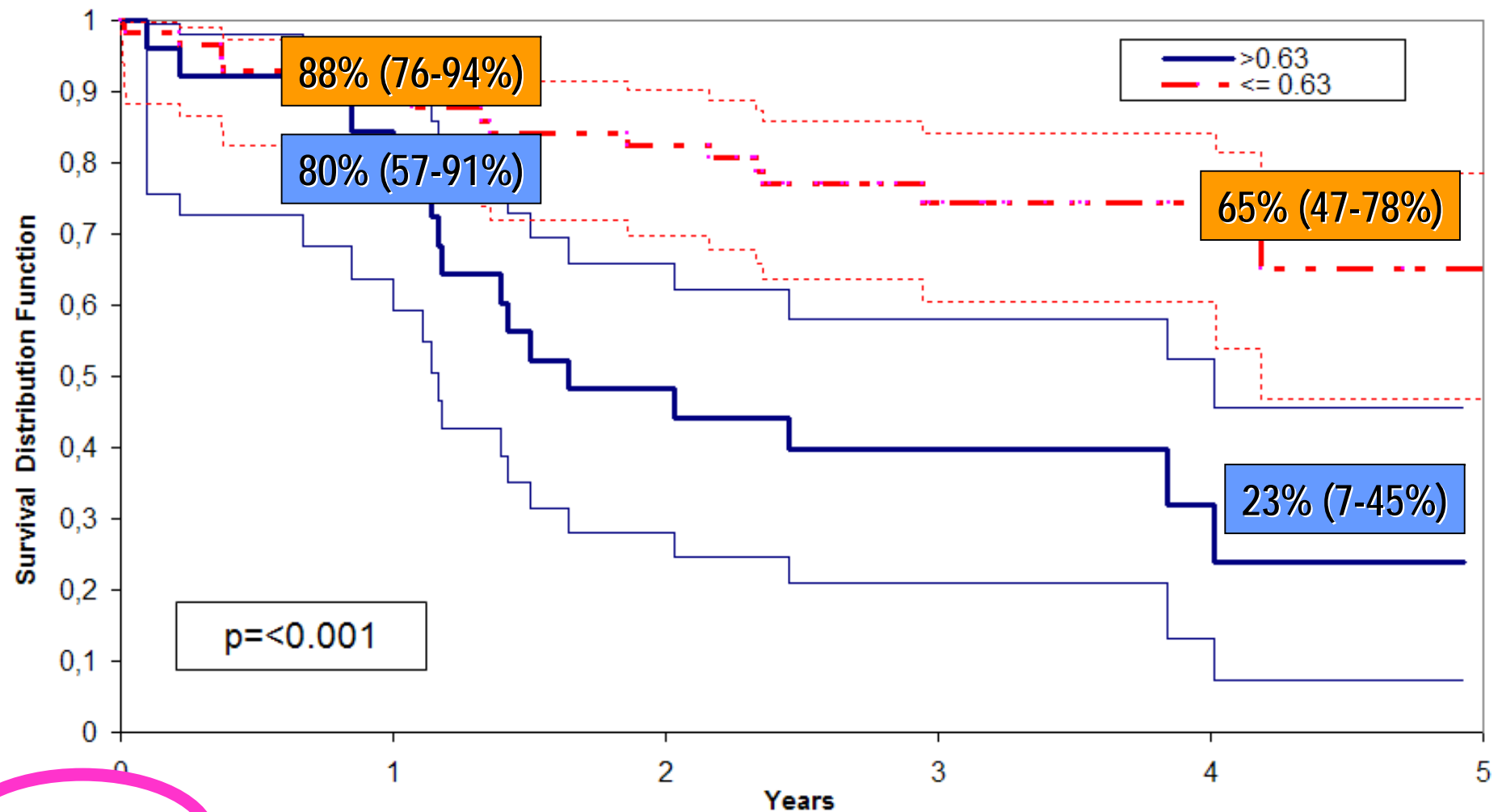
Age, gender, HIV-risk factor, HCV genotype, pre-OLT HCV viral load, Child score, CD4, CDC Stage, HCC and donor's causes of death were not associated with death.

Prognostic Risk Score of the 84 OLT in HCV-HIV-Infected Recipients

- We used MELD score, donor age and OLT-HIV volume center variables to know the individual risk (Hazard ratio) of death of the 84 recipients.
- All cases were sorted according their individual risk score from low to high.
- The **risk score** which separate 50% of deaths classified the 84 recipients as having a low or a high risk of death (**0.63**).
- KM survival curves were done and analyzed by log-rank test.

Summary of the Number of Censored and Uncensored Values					
Stratum	score5z	Total	Failed	Censored	Percent Censored
1	>0.63	27	17	10	37.04
2	<= 0.63	57	16	41	71.93
Total		84	33	51	60.71

Survival After OLT in HCV-HIV-Infected Patients (N=84) According to a Prognostic Risk Score (High vs. Low)



Patients at risk

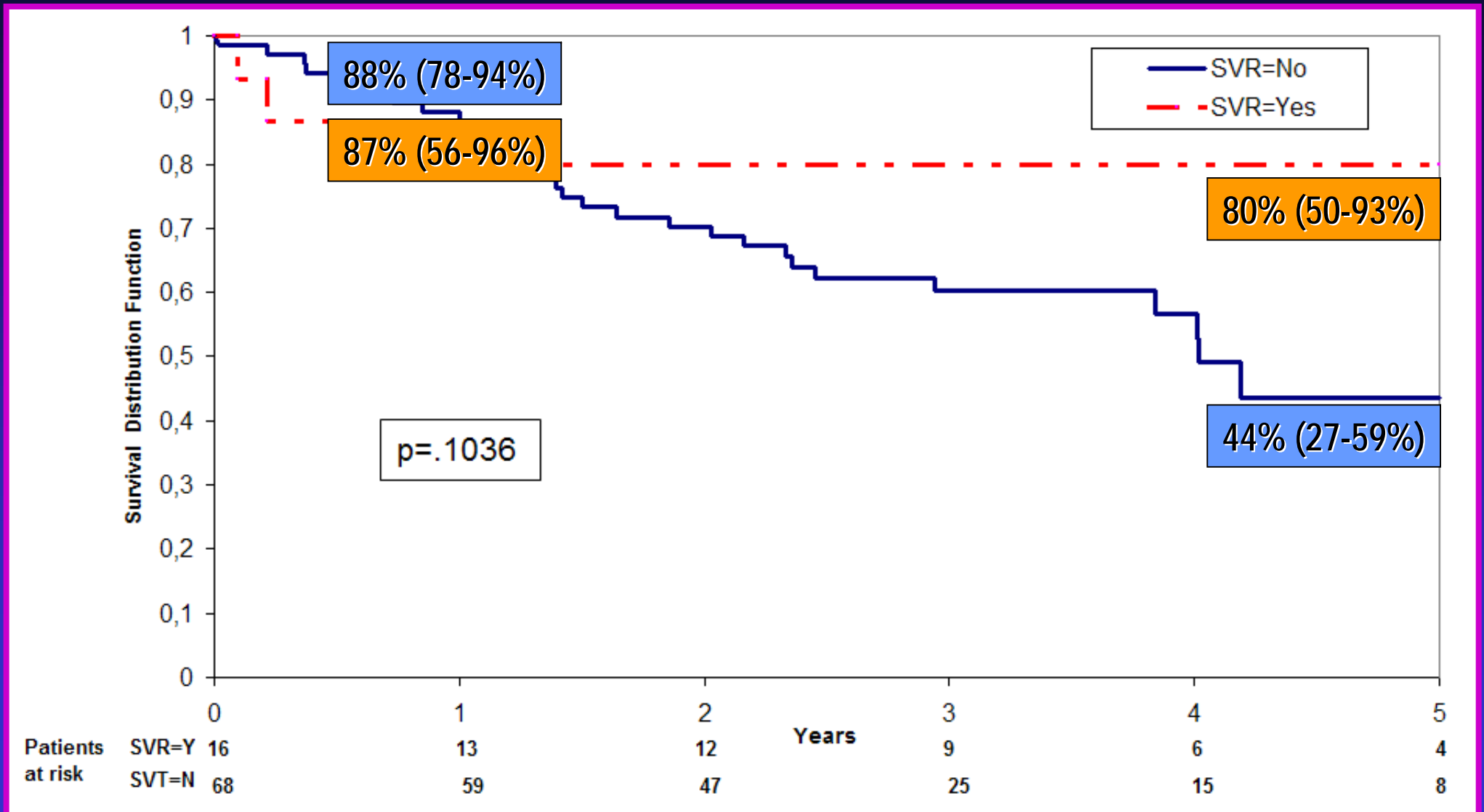
>0.63

27

<=0.63

57

Survival After OLT in HCV/HIV-Coinfected Patients According to Negative HCV RNA (Pre-OLT or SVR)



Conclusions

- 1-year and 5-year survival of OLT in HIV/HCV-coinfected recipients was 88% and 52%, respectively.
- OLT in HIV/HCV-coinfected recipients had a lower medium-term (5 years) survival than the matched HCV-monoinfected recipients (69%).
- A high MELD score, a donor age >60 yr. and a low OLT-HIV volume center were the pre-OLT variables associated with death.
- A prognostic risk score done with these three variables identified that 2/3 of cases had a 5-year prognosis (65%) as good as in HCV-monoinfected (69%) matched recipients.

ACKNOWLEDGMENTS

- Fundación para la Investigación y Prevención del SIDA en España (FIPSE).
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- Fundación SEIMC-GESIDA (FSG)
- Secretaria del Plan Nacional del Sida (SPNS) del Ministerio de Sanidad y Consumo (MSC).
- Organización Nacional de Trasplante (ONT).

Our patients



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