

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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# Hospital Clinic – University of Barcelona, Spain

## Barcelona Hospital Clinic

### HIV cohort (1983-2009)

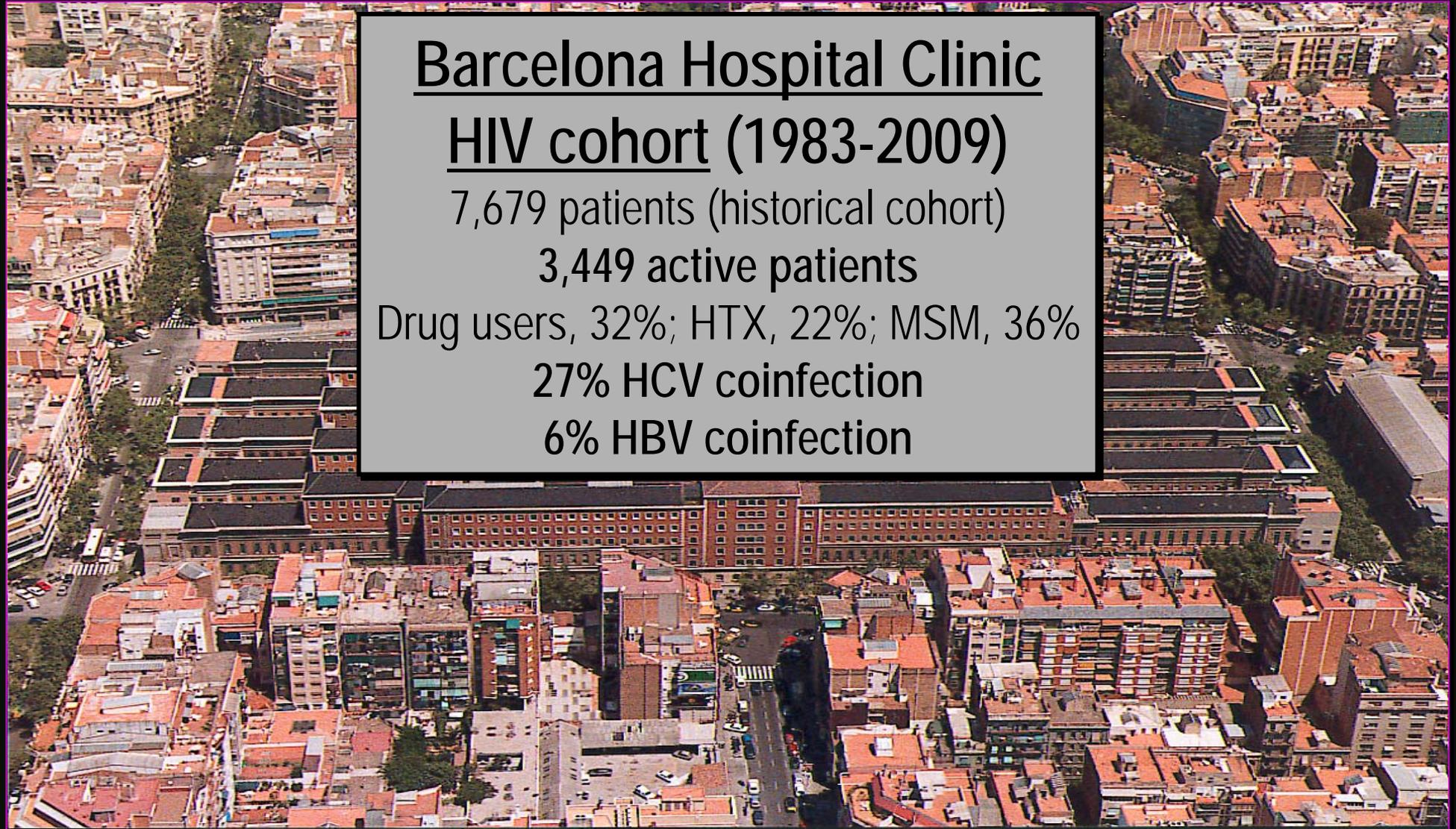
7,679 patients (historical cohort)

3,449 active patients

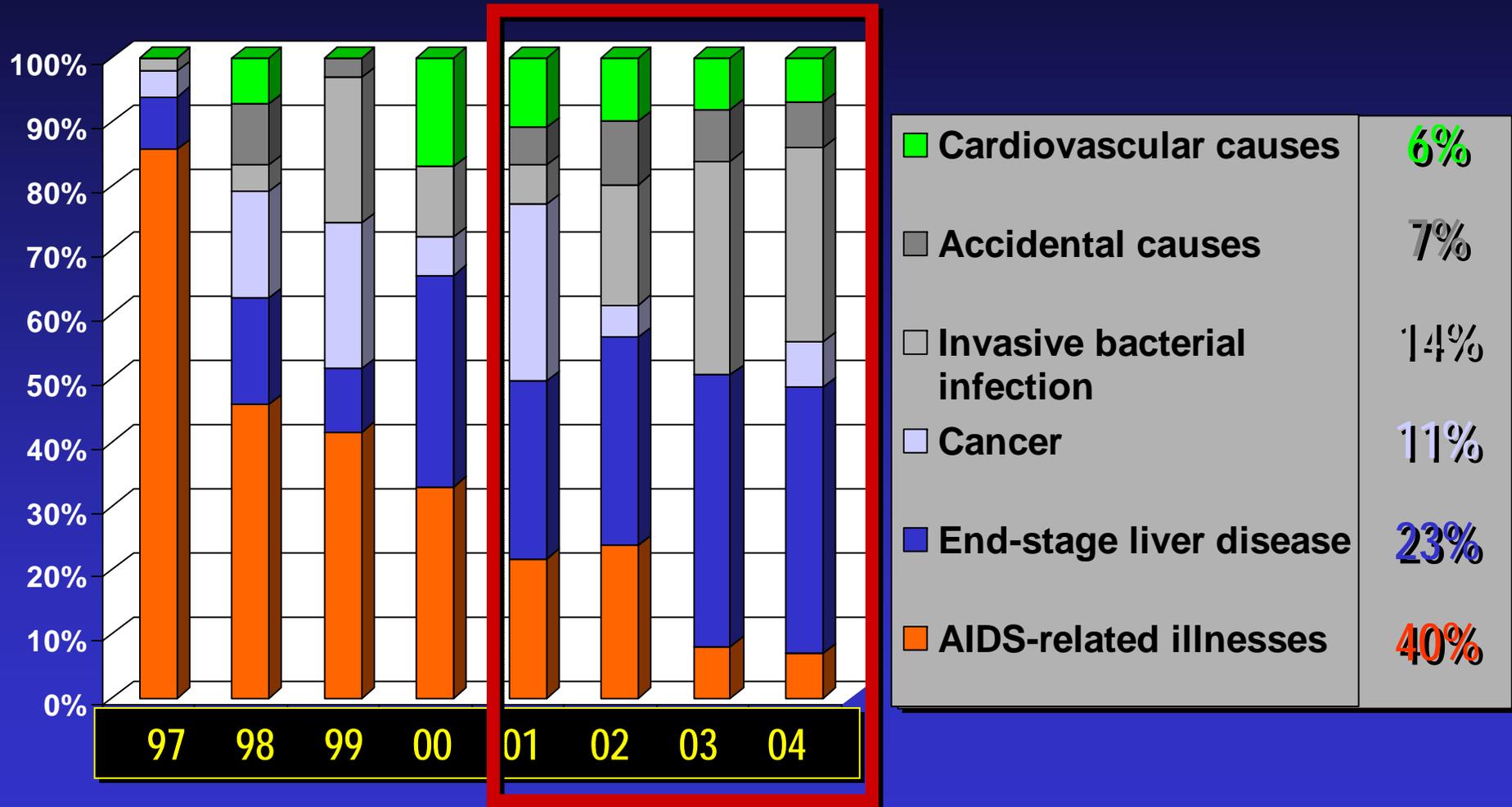
Drug users, 32%; HTX, 22%; MSM, 36%

27% HCV coinfection

6% HBV coinfection



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



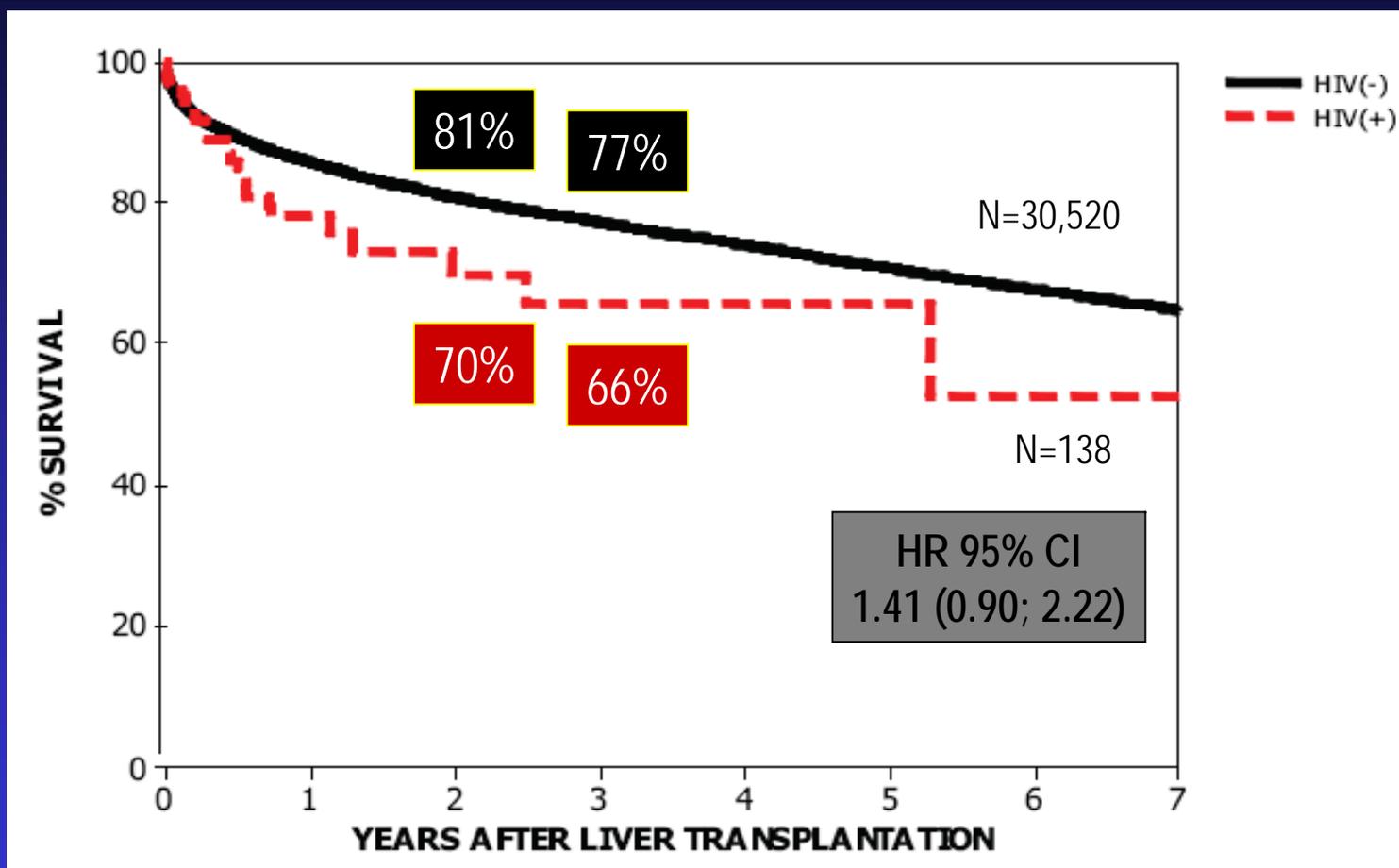
Martinez E. et al. HIV Medicine. 2007; 8: 251-258.

# 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)

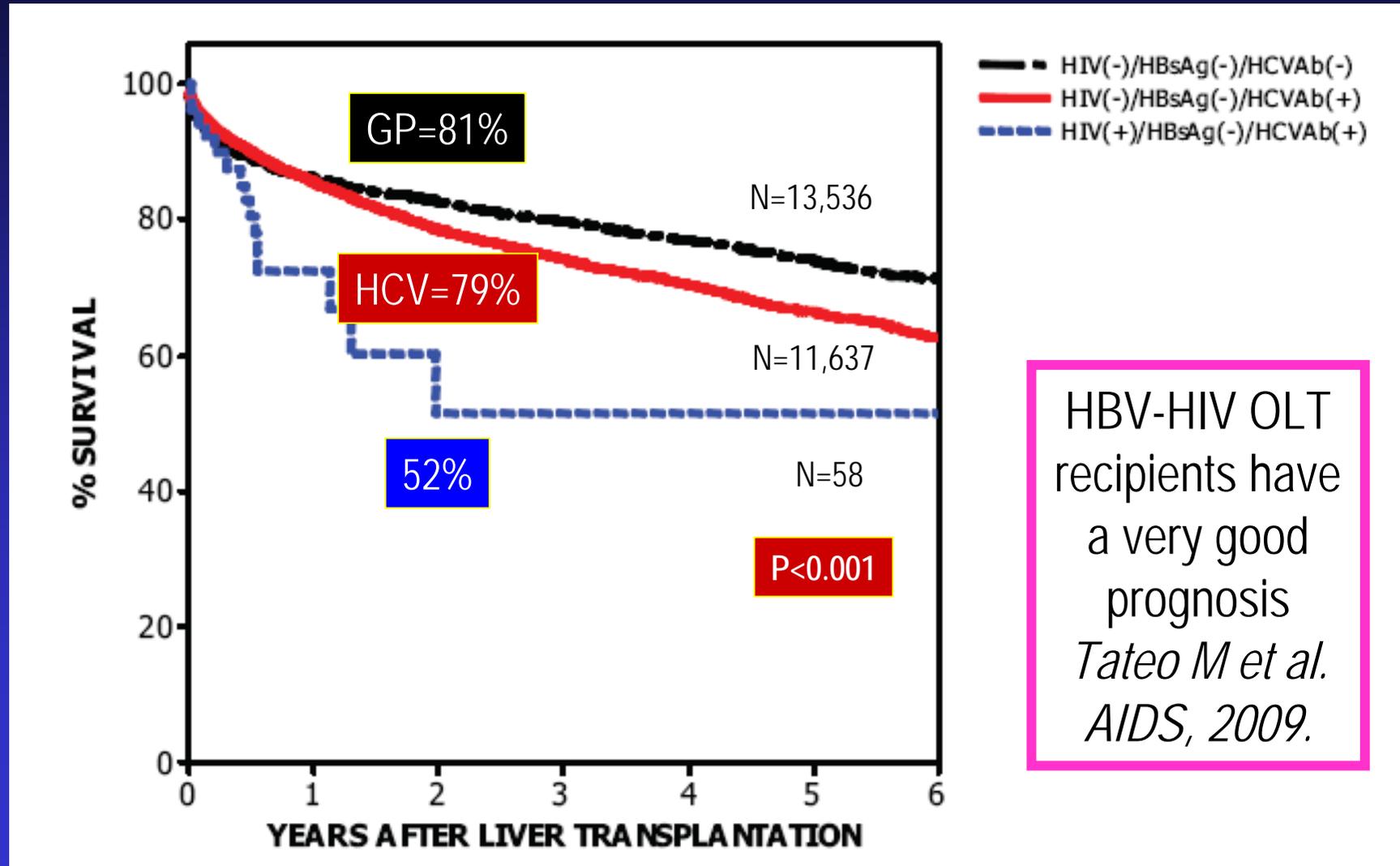
Mindikoglu AS et al. Transplantation 2008;85: 359–368.



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.

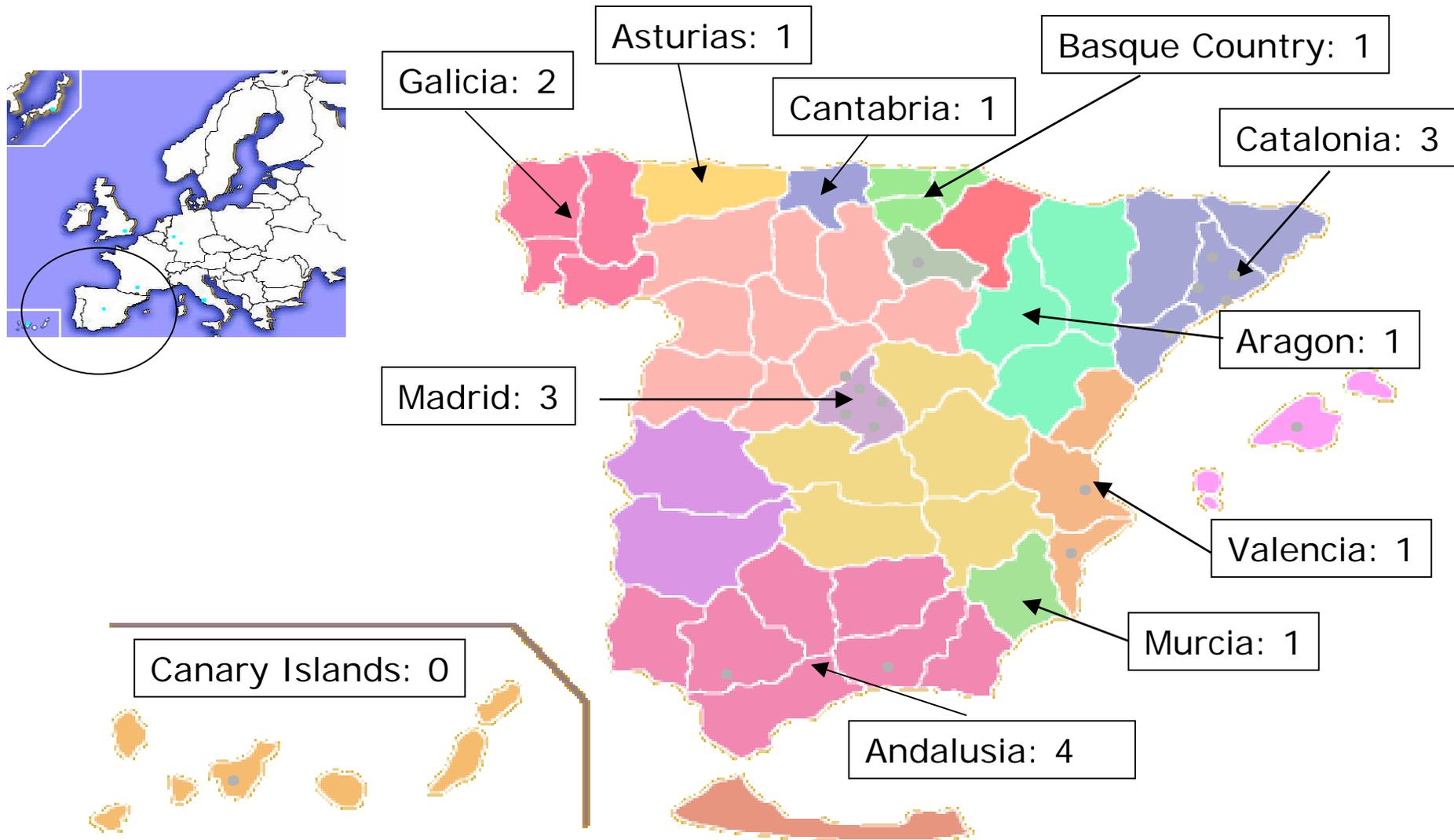
## OBJECTIVE

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/mm<sup>3</sup> 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 ( $\pm 12$  years), gender, calendar year ( $\pm 1$  year), HBV coinfection, and presence of hepatocellular carcinoma.
  - Data for HIV-negative recipients were obtained from the SETH database.

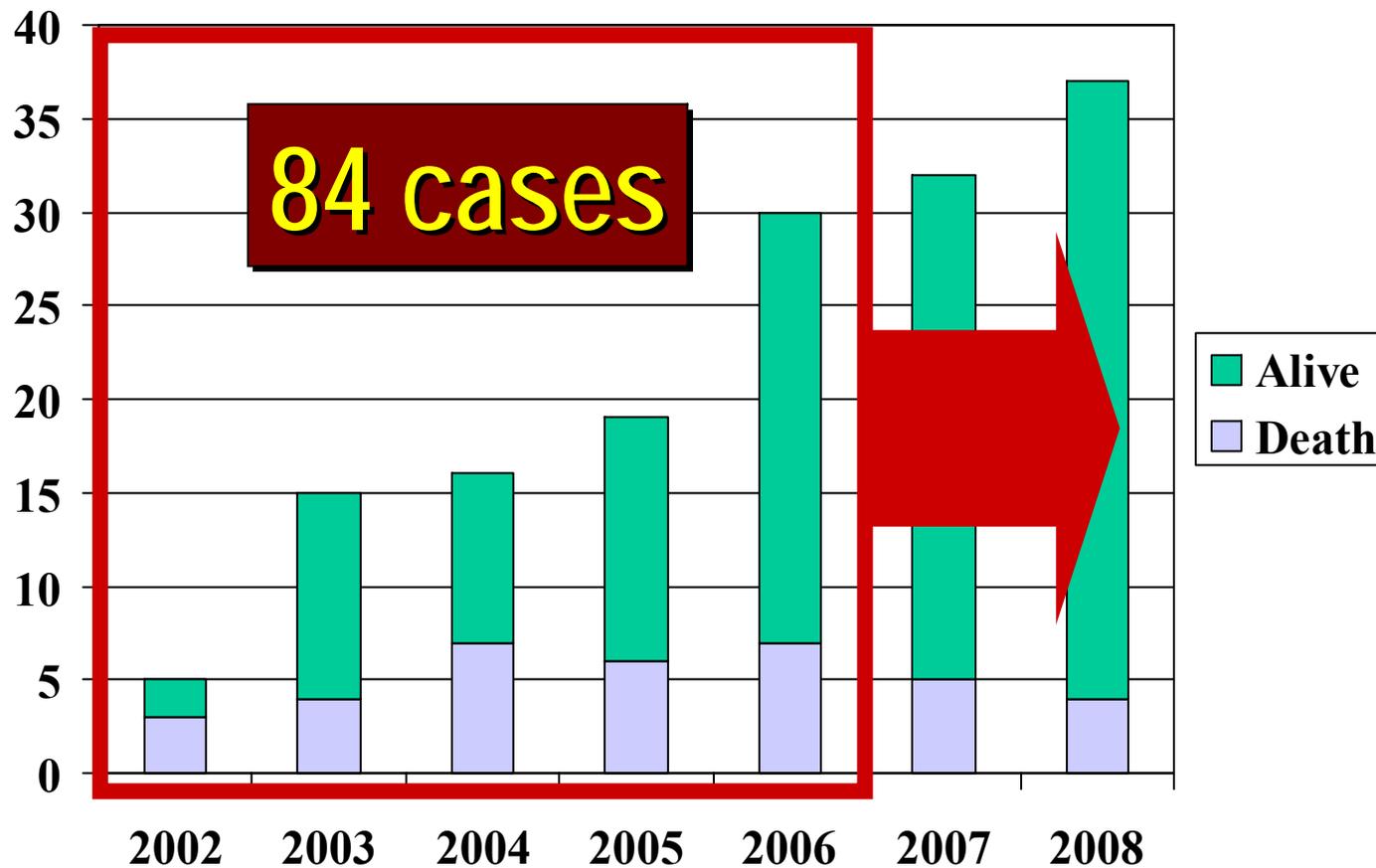
# Limitations of the Control Group (N=252)

- 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)

	<b>HIV+HCV N=84</b>	<b>HCV N=252</b>
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

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

\* Median; \*\* Hepatocellular carcinoma.

# Donor and Recipient Characteristics

**HIV+HCV**  
**N=84**

**HCV**  
**N=252**

## Donor

- Age >60 years	37%	29%
- Gender (males)	57%	66%

## Recipient

- Pre-OLT MELD score	15	15
- HCV Genotype 1/4	69%	75%
- SVR	19%	23%

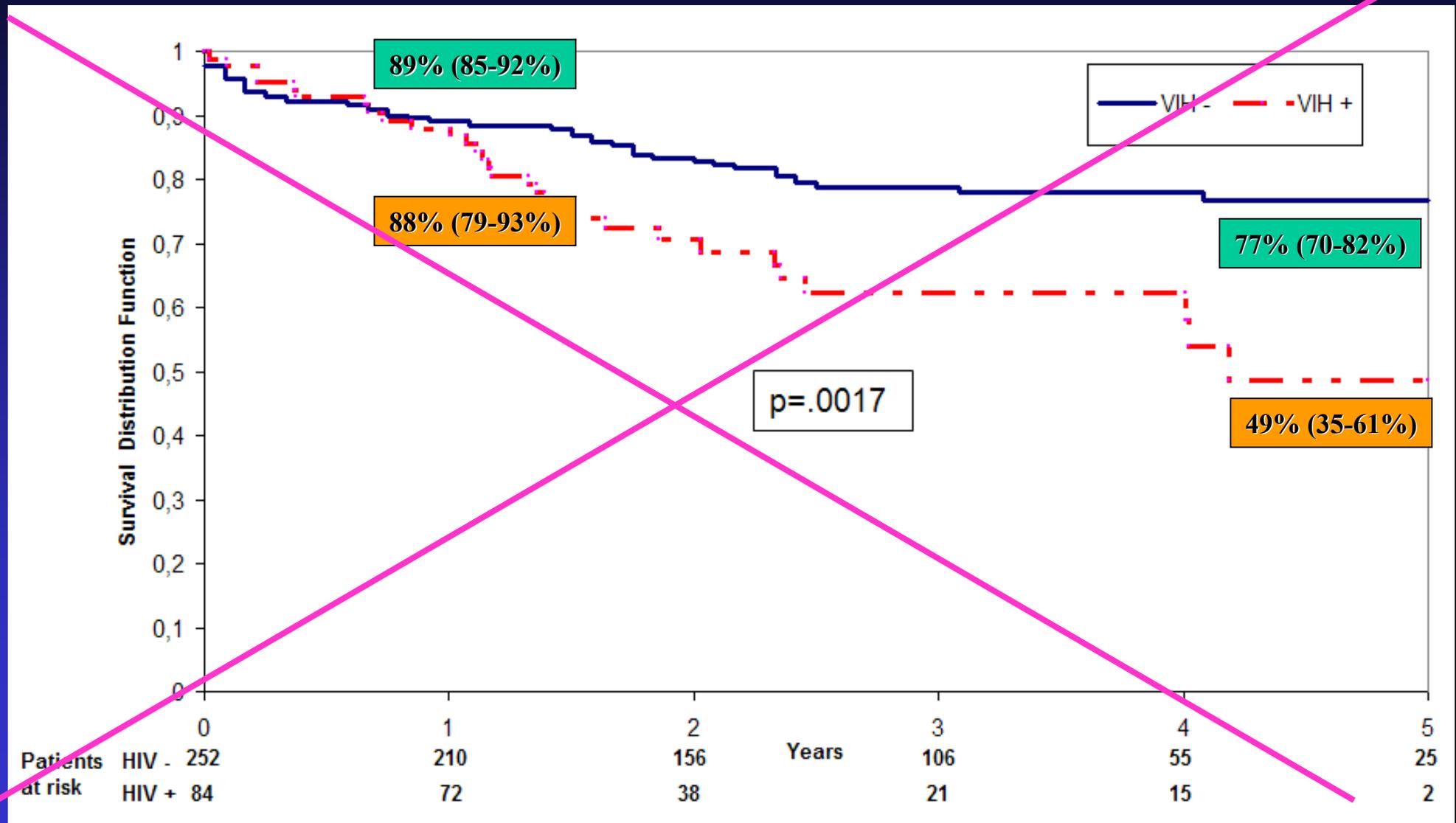
SVR = Sustained virological response.

# Causes of Death in HIV+ and HIV- Recipients

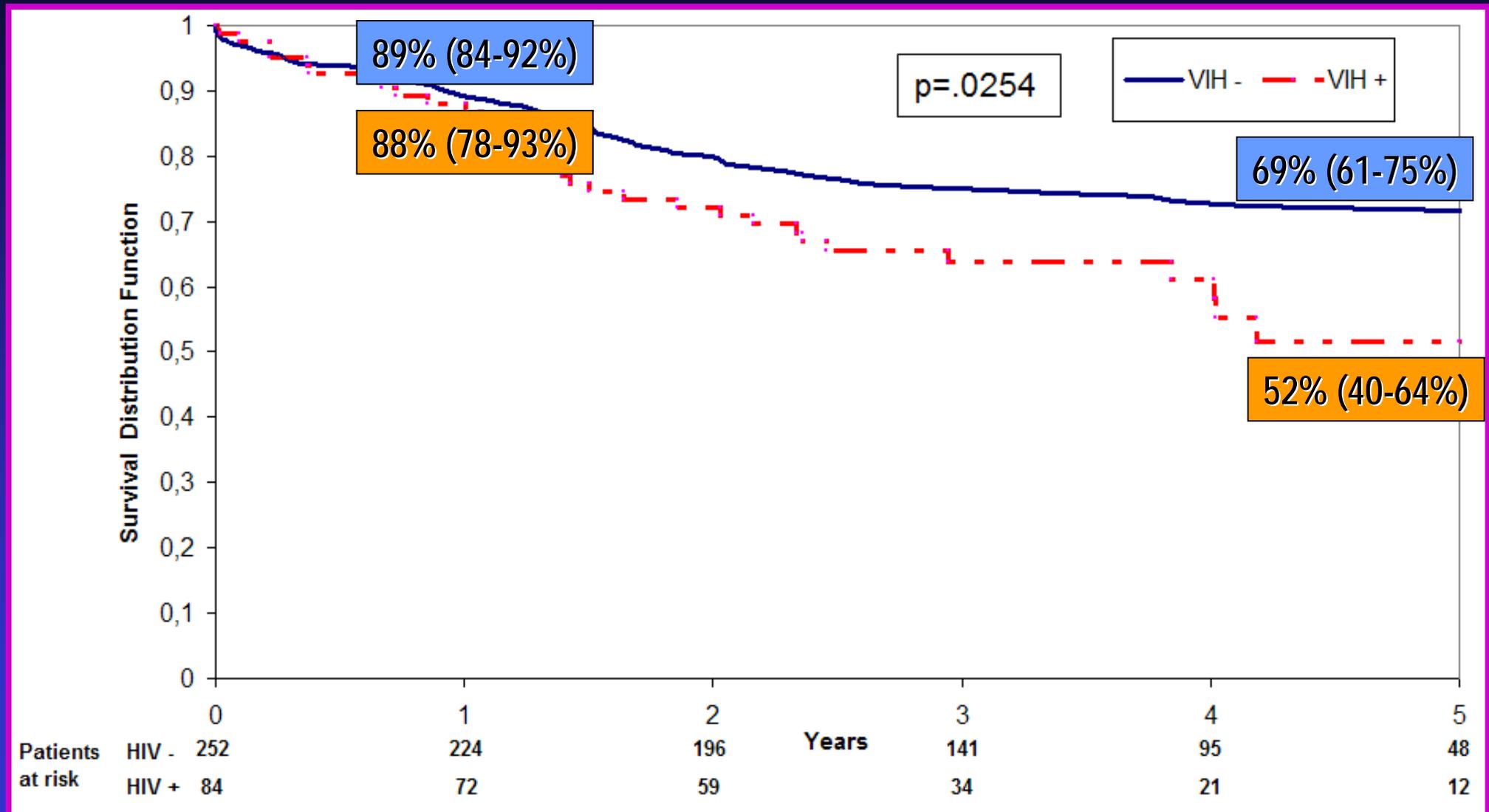
	HIV+HCV N=33	HCV N=69
Infections	20%	18%
<b>HCV recurrence</b>	<b>47%</b>	<b>42%</b>
Cancer	7%	4%
Technical complications	(-)	8%
Other	33%	28%

\* 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
<b>MELD score</b>		
- Pre-OLT (1 unit increase)	1.10 (1.03; 7.69)	.002
<b>No. of OLT per Site</b>		
- > 5 transplants	1	
- ≤ 5 transplants	4.54 (2.00;10.3)	<.001
<b>Donor age</b>		
- < 60 years	1	
- ≥ 60 years	2.16 (1.04;4.;49)	.04

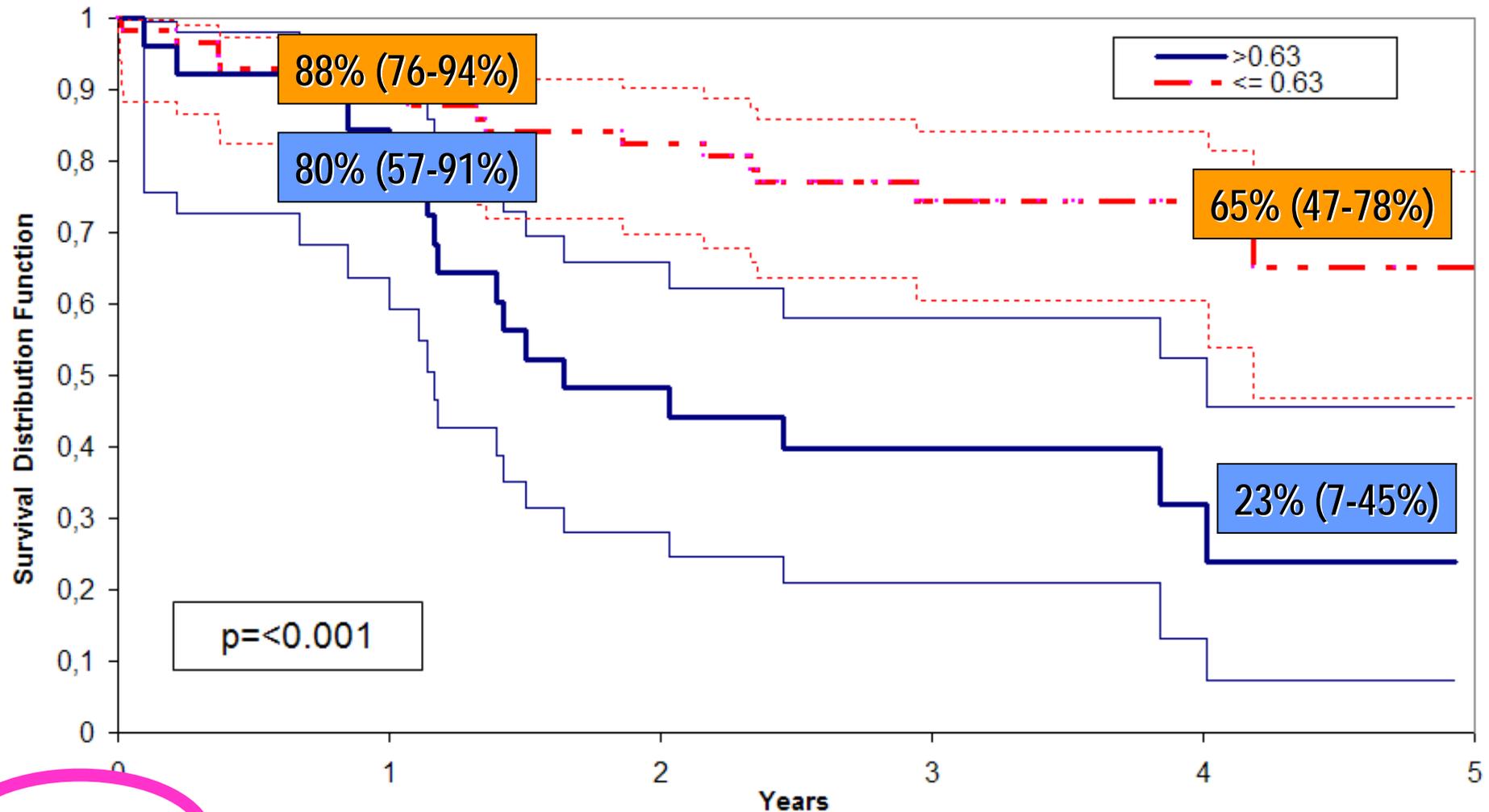
Age, gender, HIV-risk factor, HCV genotype, pre-OLT HCV viral load, Child score, CD4, CDC Stage, HCC and donor's causes of death were not associated with death.

# 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.

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

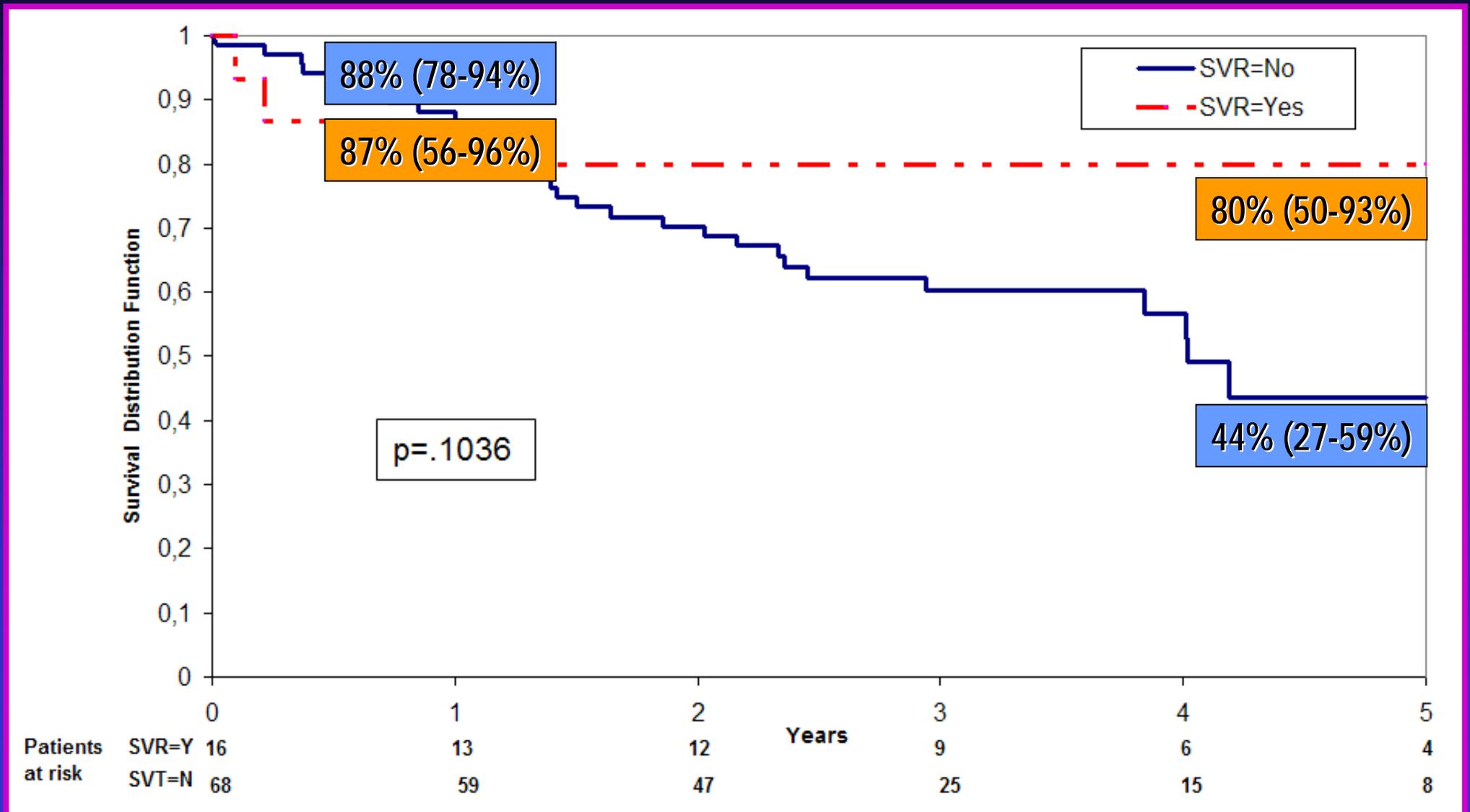
# Survival After OLT in HCV-HIV-Infected Patients (N=84) According to a Prognostic Risk Score (High vs. Low)



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).
- Grupo de Estudio de Sida (GESIDA/SEIMC).
- Sociedad Española de Trasplante Hepático (SETH).
- Grupo de Estudio de Infecciones en Trasplantados. (GESITRA/SEIMC).
- 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



# I Congreso *GeSIDA*

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