Long-term Immunity of an Inactivated Hepatitis A Pediatric Vaccine 80U in Argentinean children from an Intermediate-High Endemicity Area.

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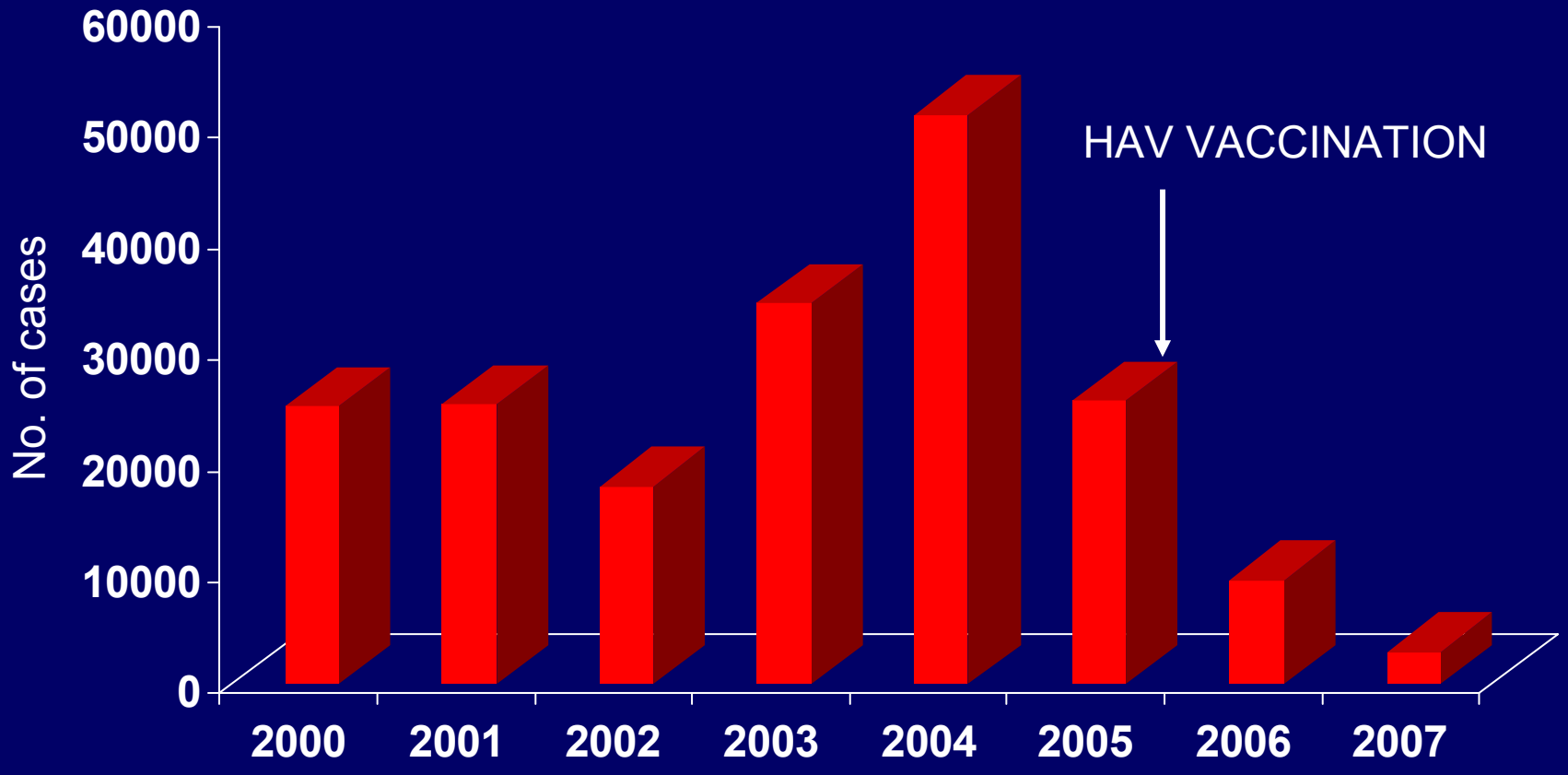
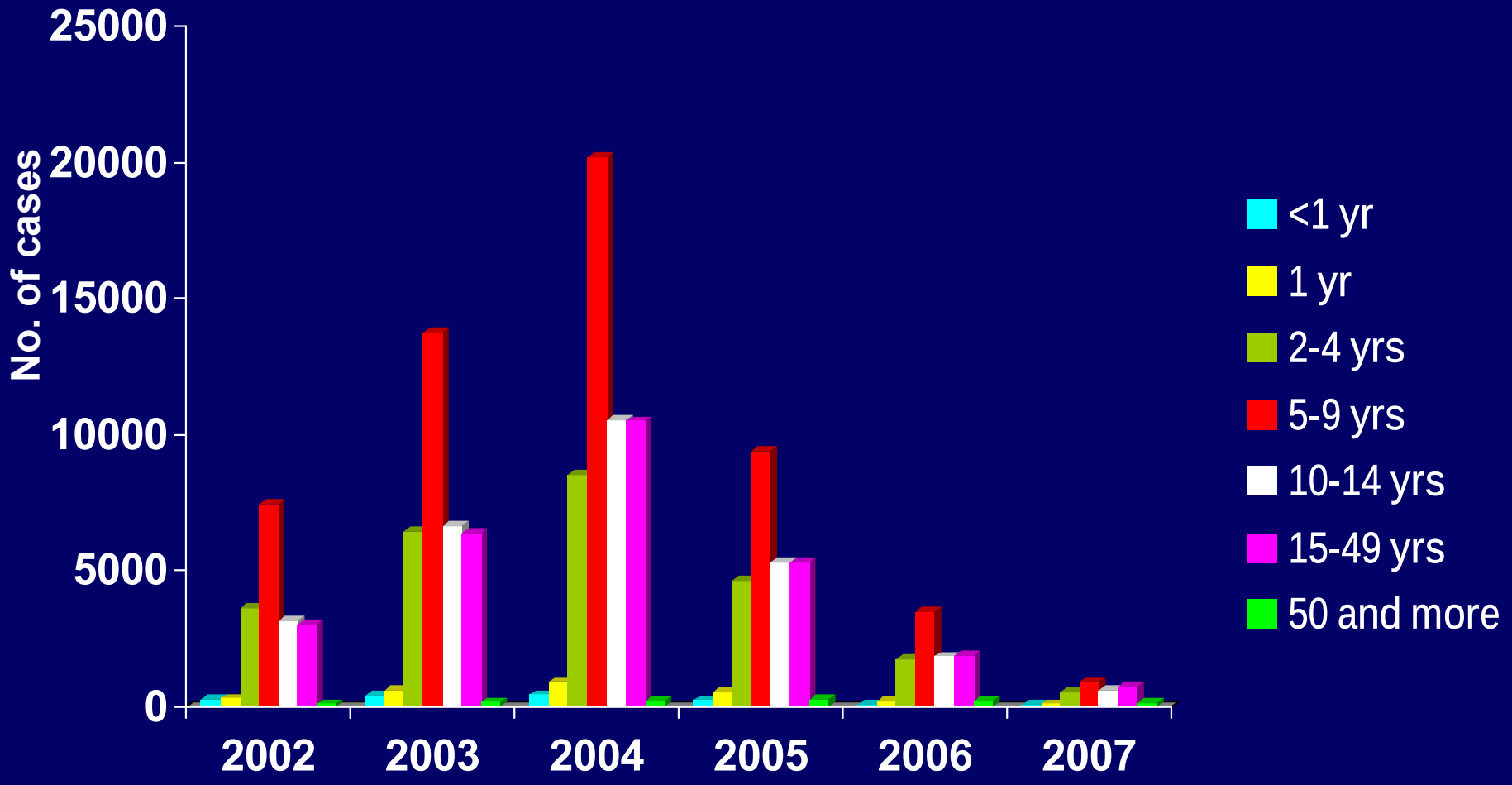
Dr. E. L. López is a consultant of Sanofi Pasteur, Argentina

OFFICIAL CONFIRMED HEPATITIS A CASES IN ARGENTINA*

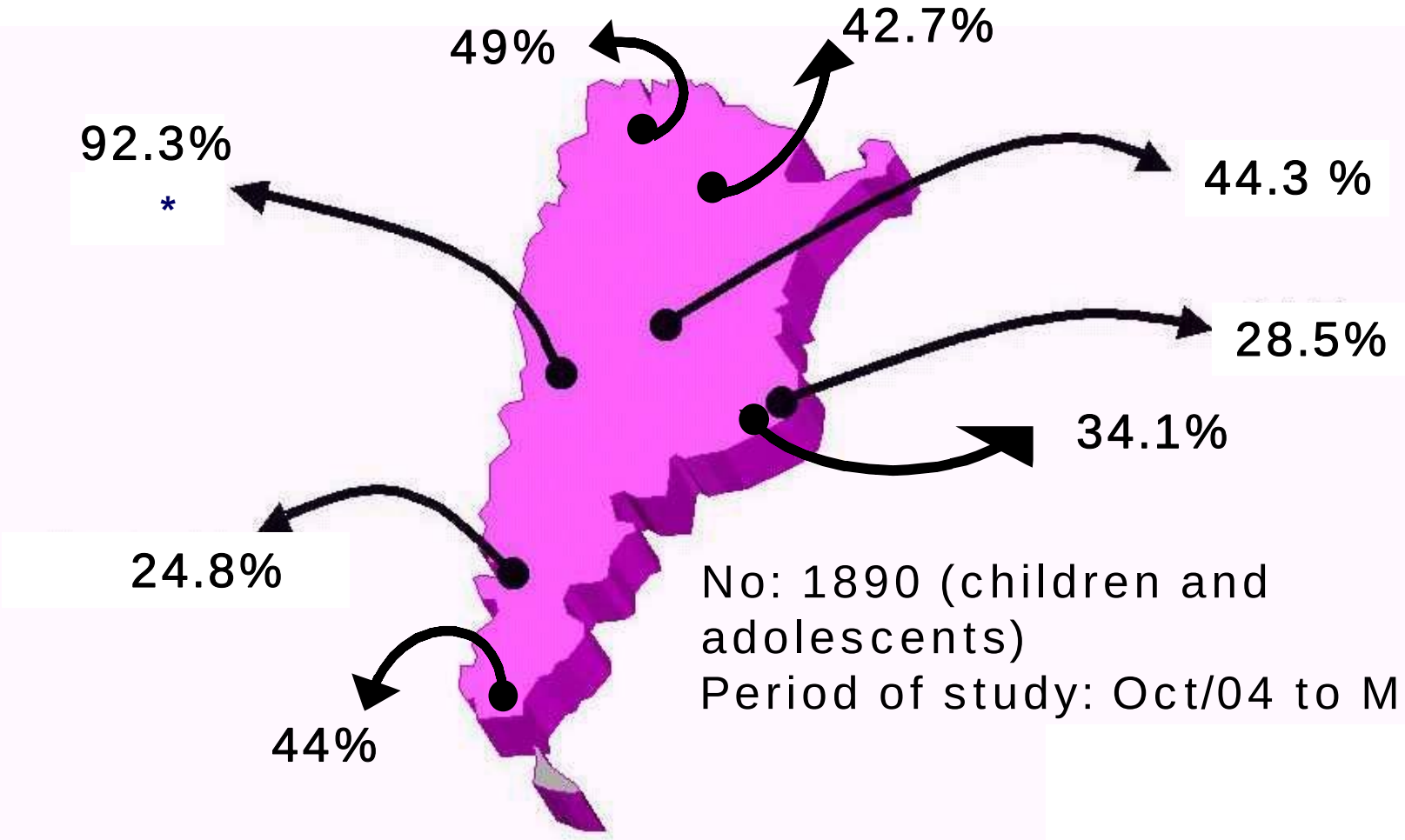


* DIEPI MINISTERY OF HEALTH

HEPATITIS A CASES BY AGE – 2002/07
MINISTERY OF HEALTH DATA



NATIONWIDE SEROPREVALENCE STUDY IN DIFFERENT ARGENTINEAN AREAS

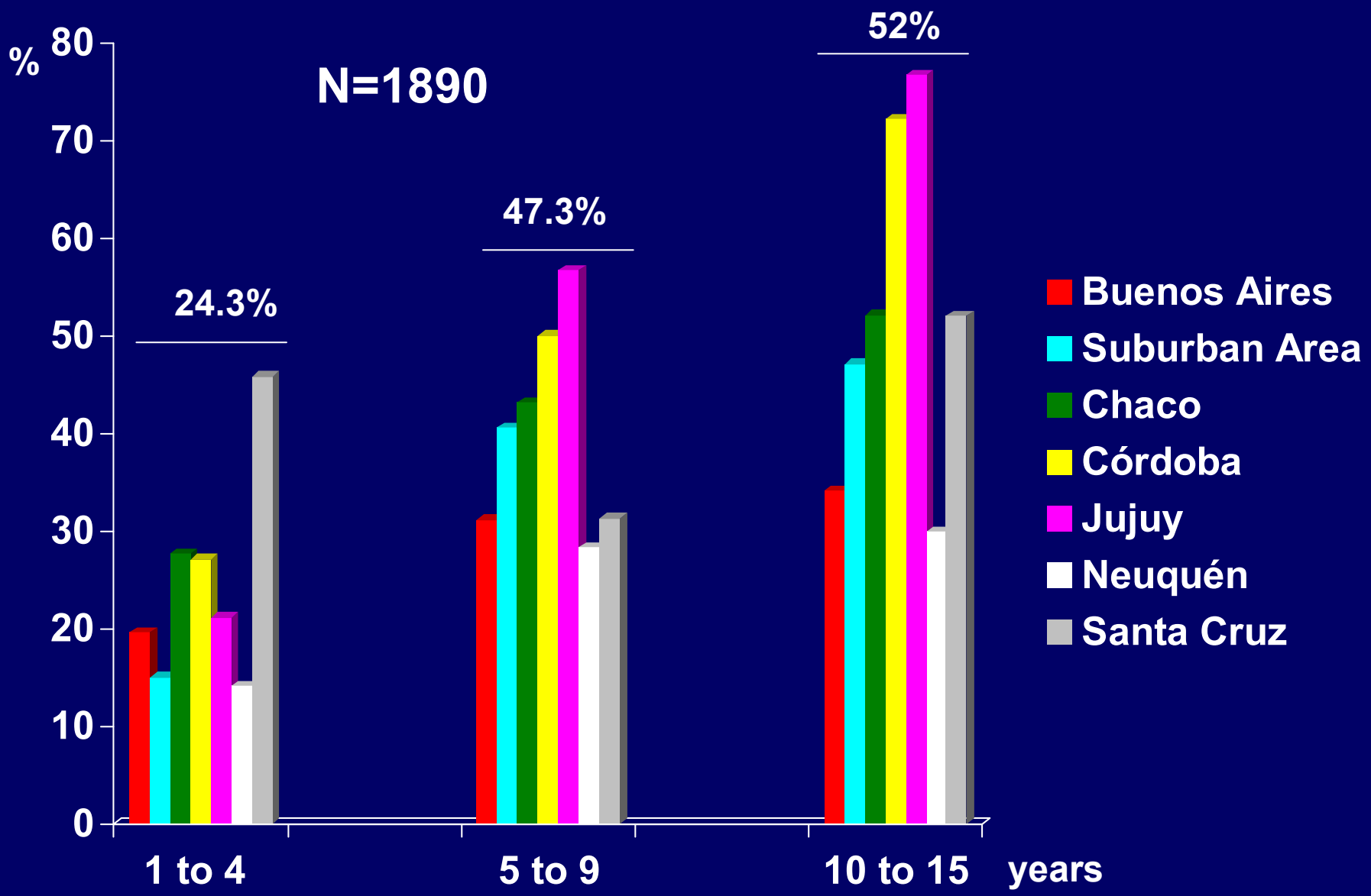


No: 1890 (children and adolescents)
Period of study: Oct/04 to Mar/ 05

*** Severe Outbreak occurred in Mendoza, during the Study – 2004-2005**

Lopez EL et al: Abstract presented at SLIPE Congress Veracruz, Mexico 2005

Argentina Anti-HVA-Antibodies Seroprevalence by Age



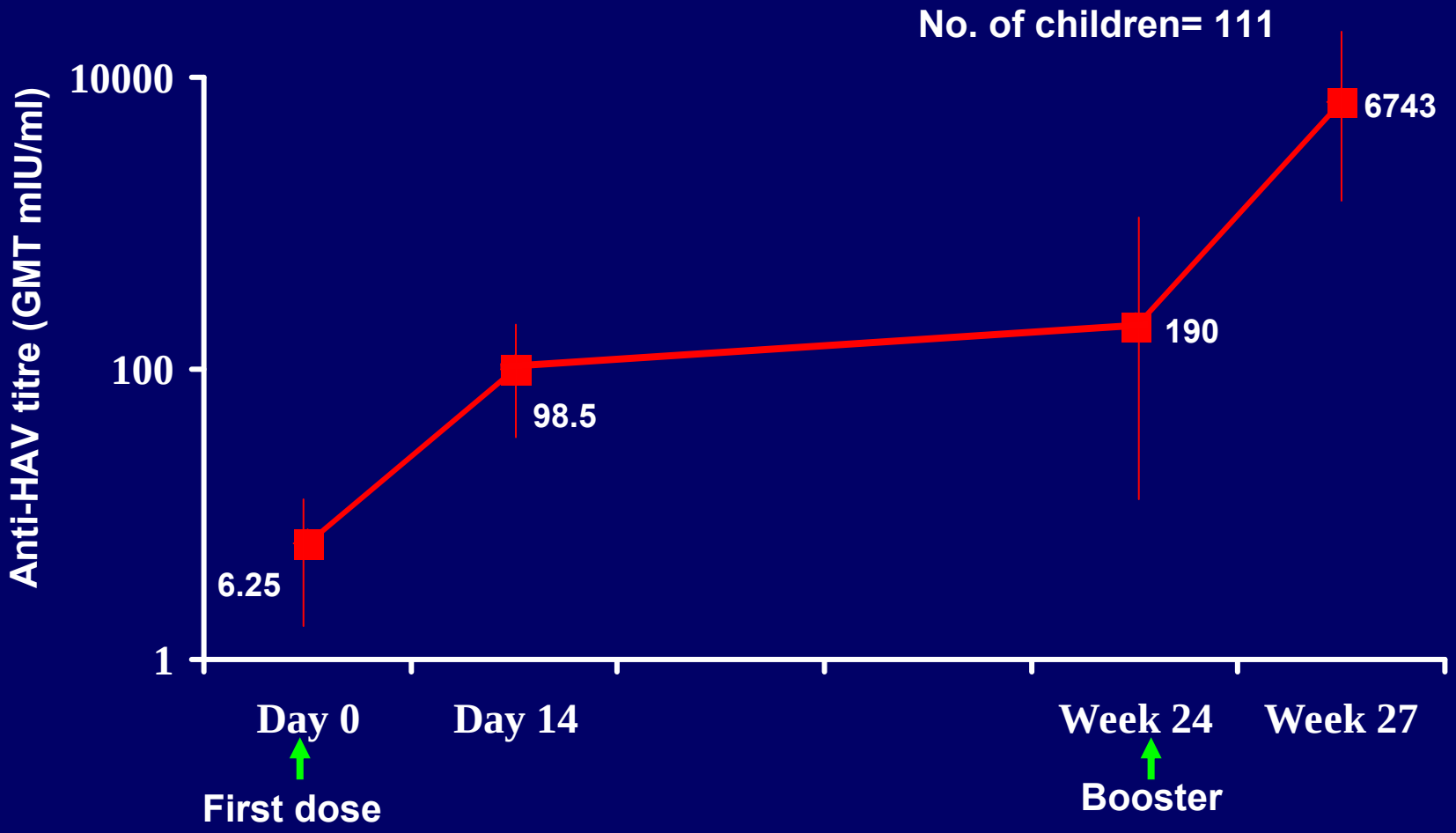
OBJECTIVE OF THE STUDY

To evaluate the long-term immunity following two doses schedule with an inactivated HAV (Avaxim 80U™) in children vaccinated at 1 to 4 years old, ten years ago.

HEPATITIS A 80 U VACCINE: INITIAL DATA OF IMMUNOGENICITY

* López EL, et al. PIDJ, 2001;20:48-52

HAV Vaccine (80U) Study Geometric Mean Titres in Initially Seronegative Subjects after Vaccination*



* López EL, et al. PIDJ, 2001;20:48-52

HAV Vaccine (80U) Study seroconversion Rates (SC) and GMT in mIU/mL in all Initially Seronegative Children

	Day 0 (n=111)	Day 14 (n=111)	Week 24 (n=107)	Week 27 (N=103)
GMT	**6.25**	**98.5**	**190**	**6743**
95% CI	5.8-6.8	86.9-112	162-224	5805-7833
% SC	**0**	**99.1**	**100**	**100**
95% CI	0.0-3.3	95.1-100	96.6-100	96.5-100

López EL, et al. PIDJ, 2001;20:48-52

Material and Methods (I)

- **Study Population**: 52/111 children who received under protocol Inactivated HAV Vaccine (80U) were controlled after 10 years of immunization.
- **Inclusion Criteria**
  - To have been enrolled in the former study
  - Have not received any HAV Vaccine after study Immunization
  - Informed Consent signed by parents / Asent by adolescents
- **Exclusion Criteria**
  - Whole blood, red blood cells and/or blood derived products transfusion during the last 6 months
  - Underlying disease that can cause immunosupresion
  - Immunosupresive therapy during the last 6 months

MATERIAL AND METHODS (II)

- Anti-HAV Antibody titres were measured by VIDAS® Anti-HAV Total (HAVT), from BioMerieux®, France.
- **Principle**: the assay principle combine a 2-step enzyme immunoassay competition method with a final fluorescent detection (ELFA).
- The patient Relative Fluorescent Value (RFV) is interpreted by the VIDAS system. Results are expressed in mIU/ml (WHO reference standard 1st Reference Preparation Hepatitis A immunoglobulin) (100 IU/ml).
- The results are interpreted as follows:

Concentration	Interpretation
<15 mIU/ml	Negative
≥15 and <20 mIU/ml	Borderline positive
≥20 mIU/ml	Positive

FOLLOW-UP RESULTS

CHARACTERIZATION OF POPULATION

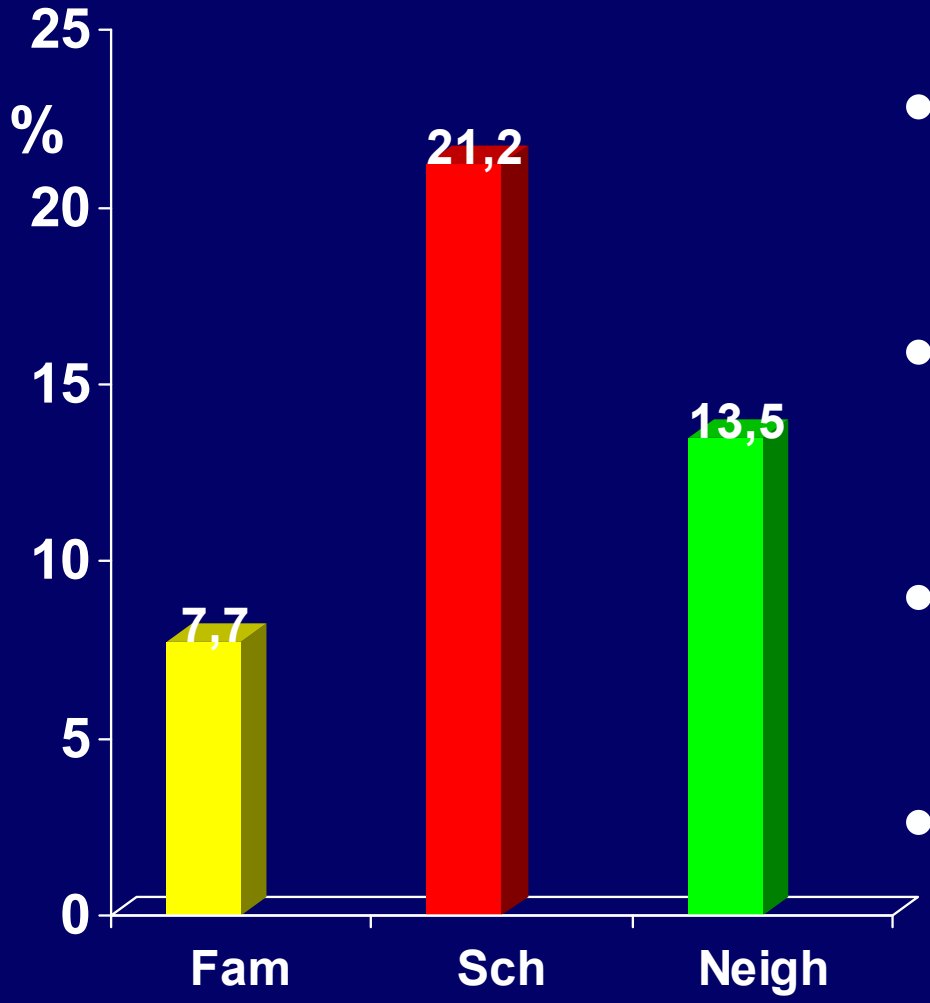
	SERONEGATIVE (n=48)*	SEROPOSITIVE (n=4)*	*p*
AGE: mo. **Mean (±SD)** **Range**	156.1 (±11.3) 137 – 176	148 (±14.9) 137 – 170	NS
SEX **Female** **Male**	26 (96.3%) 22 (88%)	1 (3.7%) 3 (12%)	NS

- **In the initial screening all subjects were seronegative by a qualitative assay before immunization, however 4 subjects were seropositive by a quantitative assay.**

HEPATITIS A VACCINEE SUBJECTS WITH HEPATITIS A CONTACT

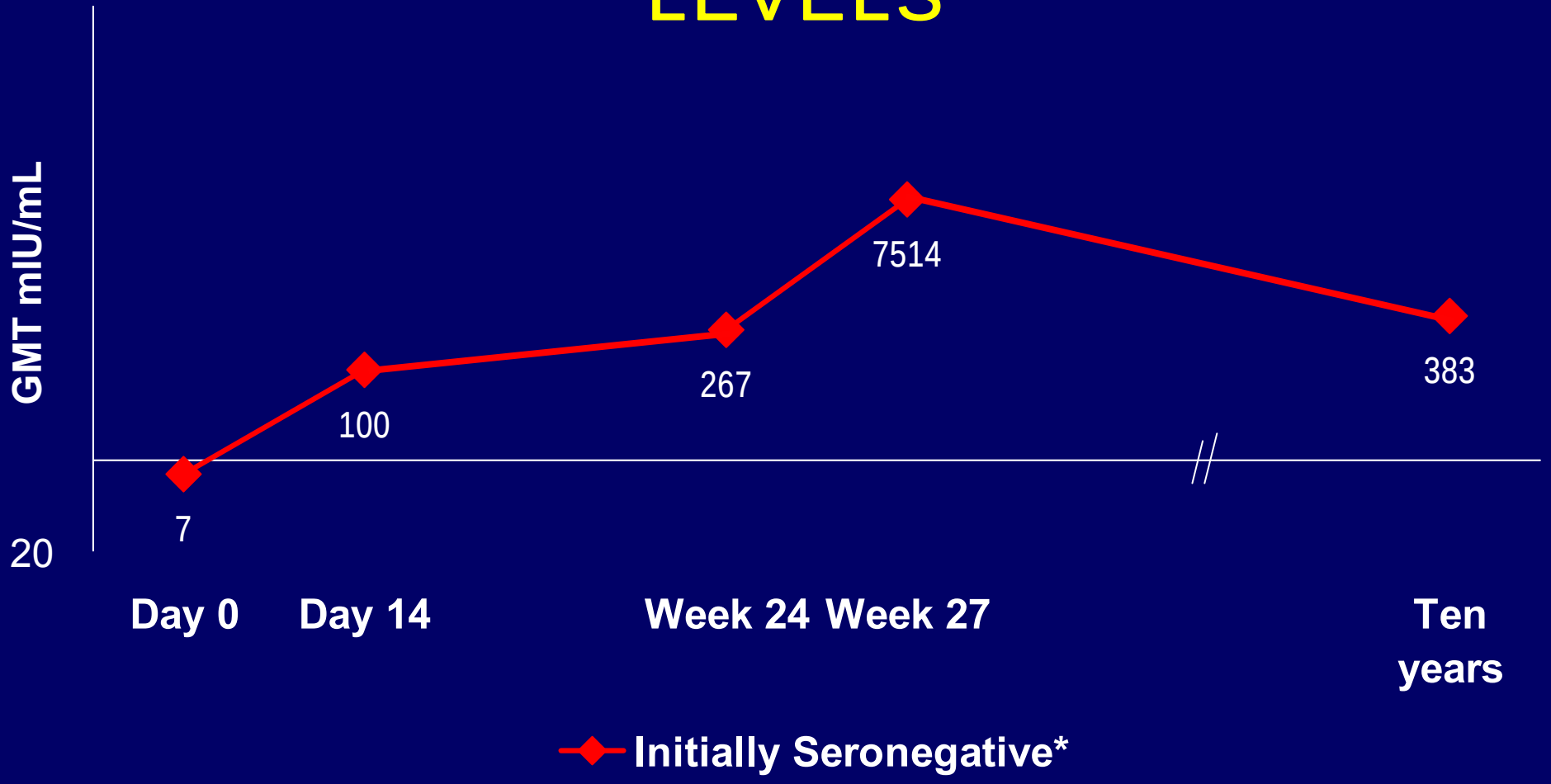
17/52 (32.7%) of subjects who had received the vaccine had an known close contact with Hepatitis A cases after vaccination

TYPE OF CONTACT



- Family: 4/52 (7.7%)
- School: 11/52 (21.2%)
- Neighborhood: 7/52 (13.5%)
- 24% of them had > 1 contact

FOLLOW-UP OF ANTI – HAV ABs LEVELS

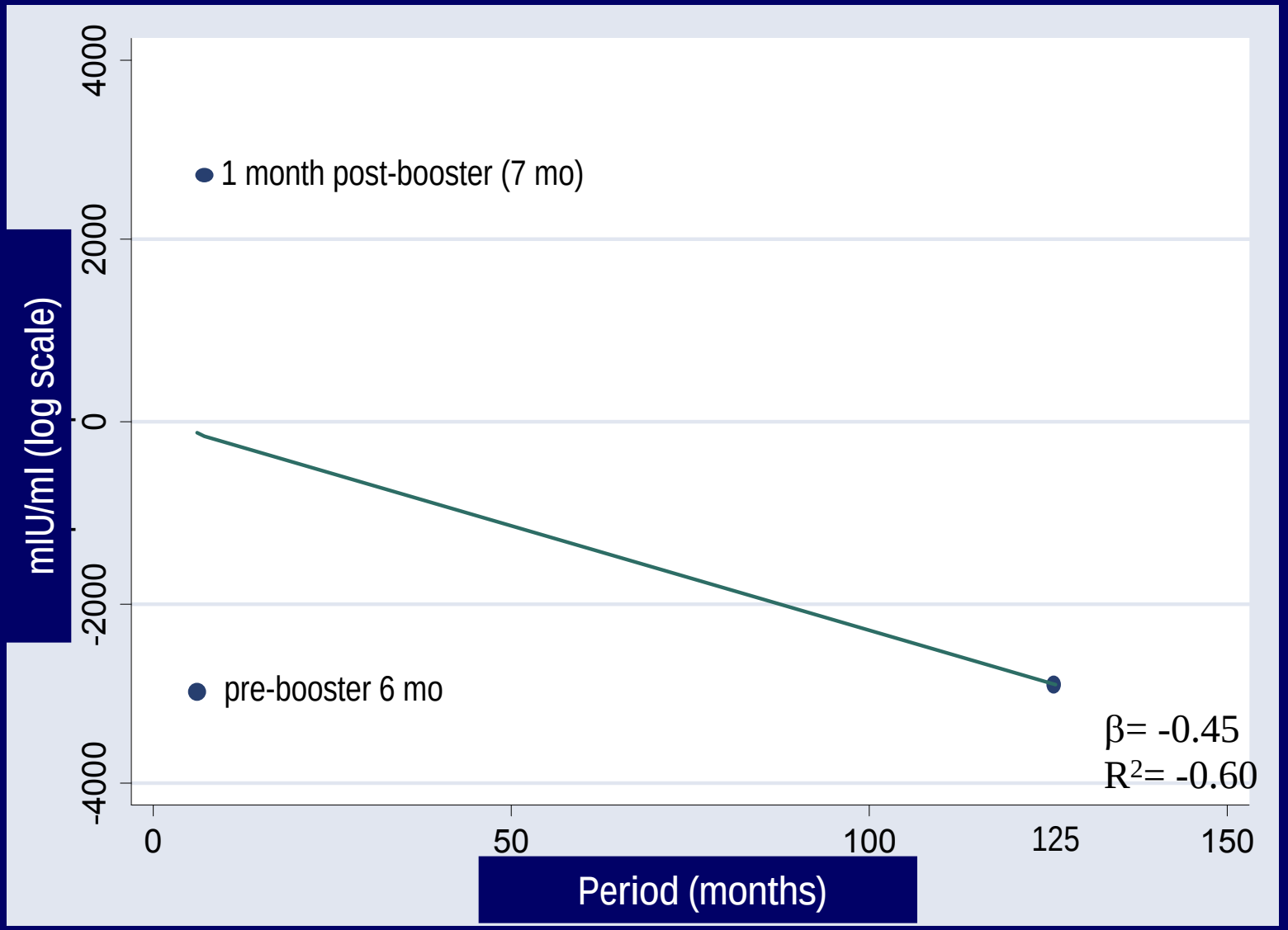


•Only 1 Subject (2.1%) who were initially Seroconverted had < 20mIU/mL at ten years follow-up.

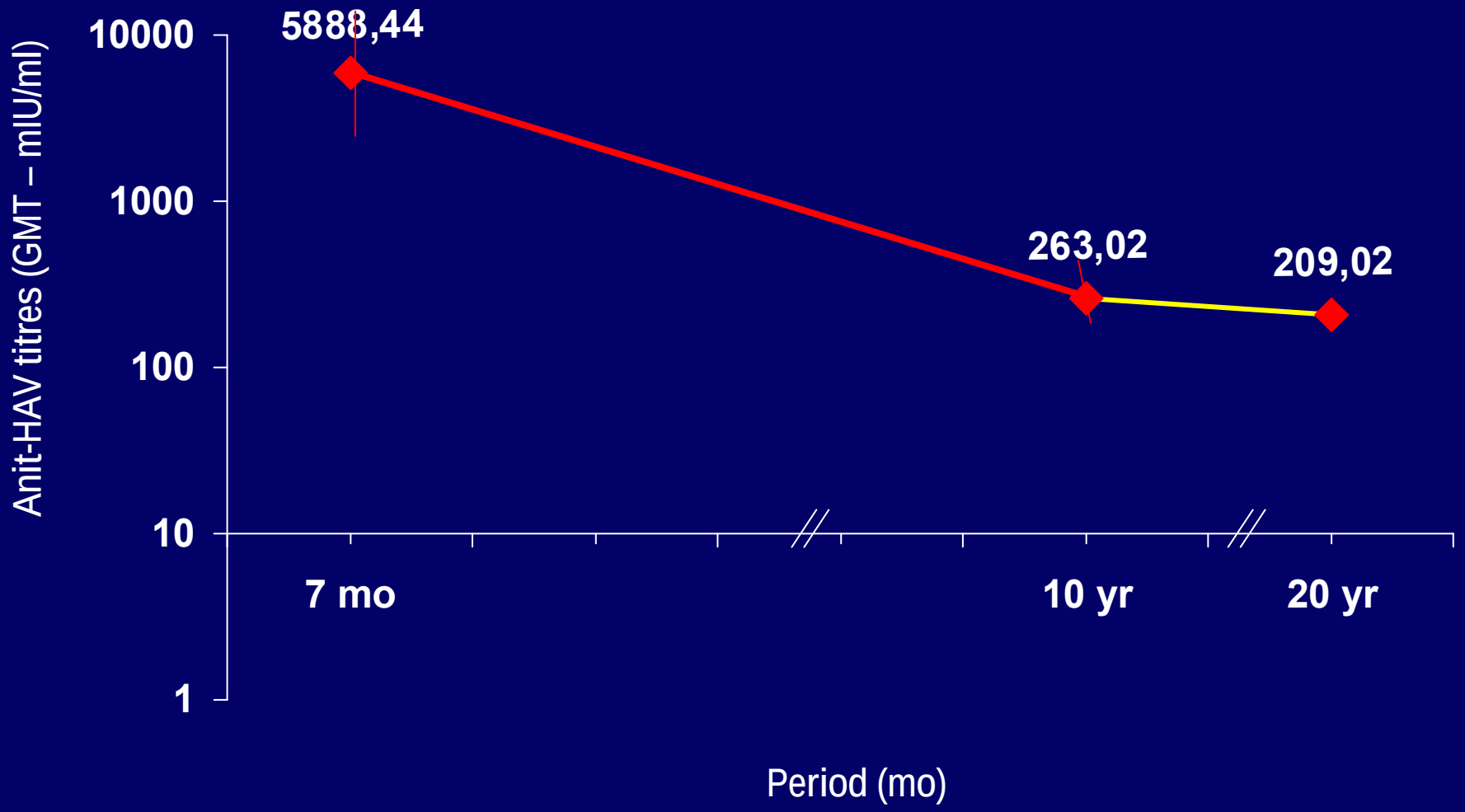
SERUM LEVELS OF ANTI-HAV AT TEN YEARS FOLLOW-UP

CONDITION	VALUE Mean (±SD)	95%CI	*p (M-W)*
Initial Serol. Status			
Negative (n: 48)	390.9 (370.1)	282.2- 499.5	
SEX			
Female	430.6 (433.4)	275.9 - 641.2	0.18
Male	483.9 (825.3)	65 - 1083	
HAV CONTACT			
Any contact	445.6 (464.4)	206.8 – 684.4	0.88
No contact	455.4 (691.2)	214.2 – 696.6	

Geometric Mean Titres (GMT) anti-HAV Abs (mIU/ml) Over time by Linear Regression



PREDICTION OF ANTI-HAV AB TITRES OVER TIME BY LINEAR REGRESSION AT YEAR 20



CONCLUSIONS

- **Using Inactivated Hepatitis A vaccine (80U) the long-term immunity at 10 years follow-up showed seroprotection levels in 97.9% of children.**

- **HAV contact after vaccination did not increased the anti-HAV titres (p=0.88)**

- **There were no difference in anti-HAV titres according to gender (p=0.44).**

CONCLUSIONS (CONT.)

- **Linear Regression analysis predict seroprotection level of anti-HAV for at least 20 years after two dose HAV vaccine schedule**

- **This is the first study with this vaccine in a selected population that shows long term protection in ten years follow-up.**

- **A close and effective surveillance should be done to evaluate the need of a second dose of Hepatitis A vaccine in Argentina since 50% of children ≥5 ys old are seronegative after an important outbreak in Argentina.**

THANK YOU FOR YOUR ATTENTION