Epidemiology of HBV in France

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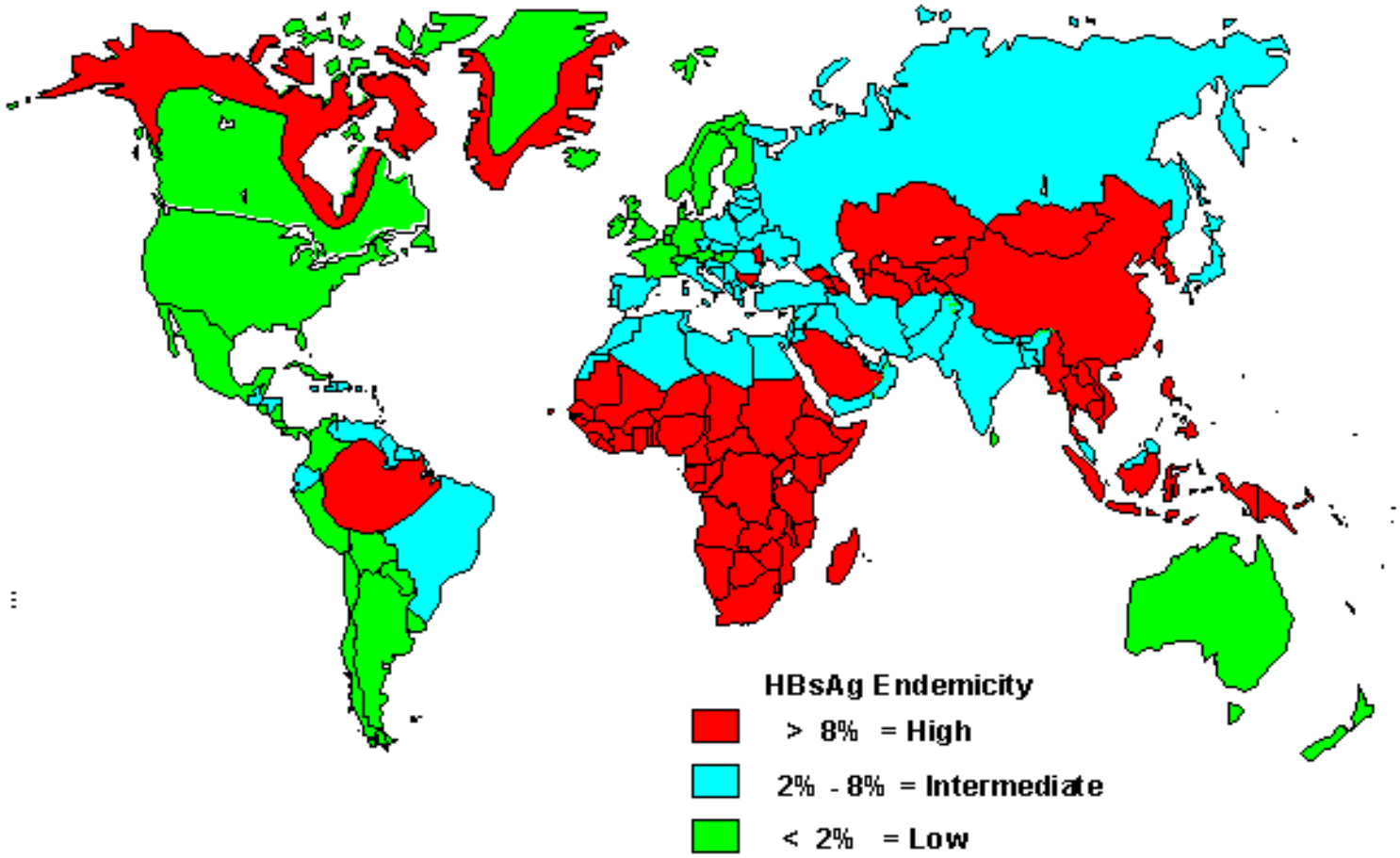
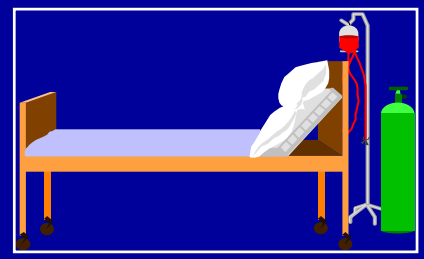
Geographic Pattern of Hepatitis B Prevalence, 1997

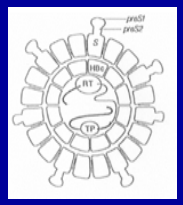


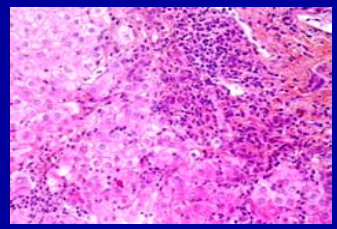
Data as of 06/04/98

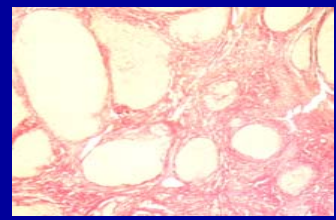
Resolution

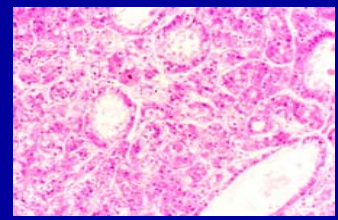


30-50 yrs









HBV → CAH → cirrhosis → HCC

Vaccine

ANTIVIRALS
IFN

IFN?

VIRAL RESISTANCE/ESCAPE

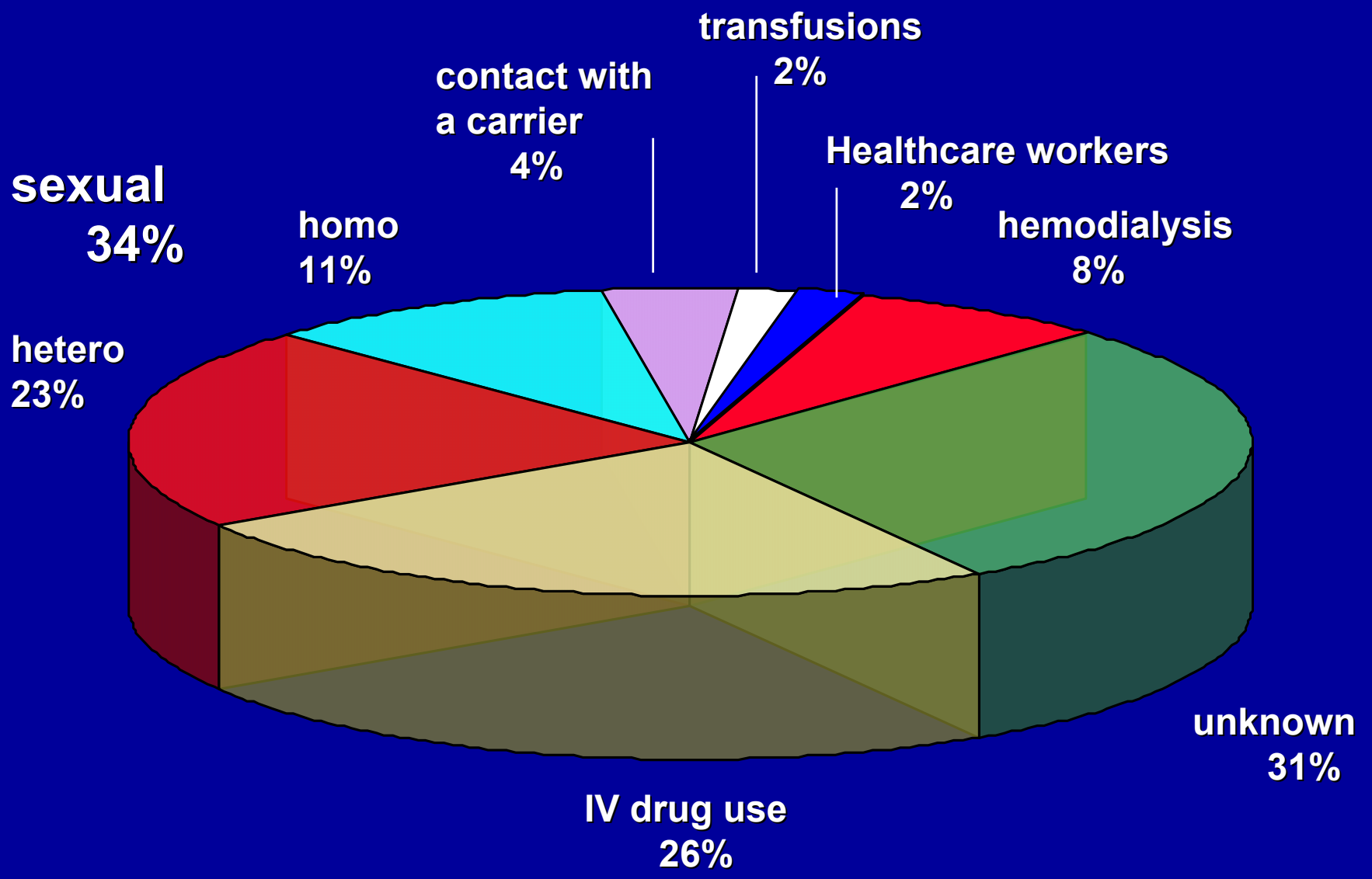
Lee, N Engl J Med 1997; Lok, Hepatology 2001

EPIDEMIOLOGY OF HBV INFECTION

IN USA

- Acute hepatitis cases
  - HAV : 40%
  - HBV : 30%
  - HCV : 20%
- incidence : 300 000 infections /year
- 30 000 new chronic carriers / year
- 3 000 death / year

TRANSMISSION OF HBV



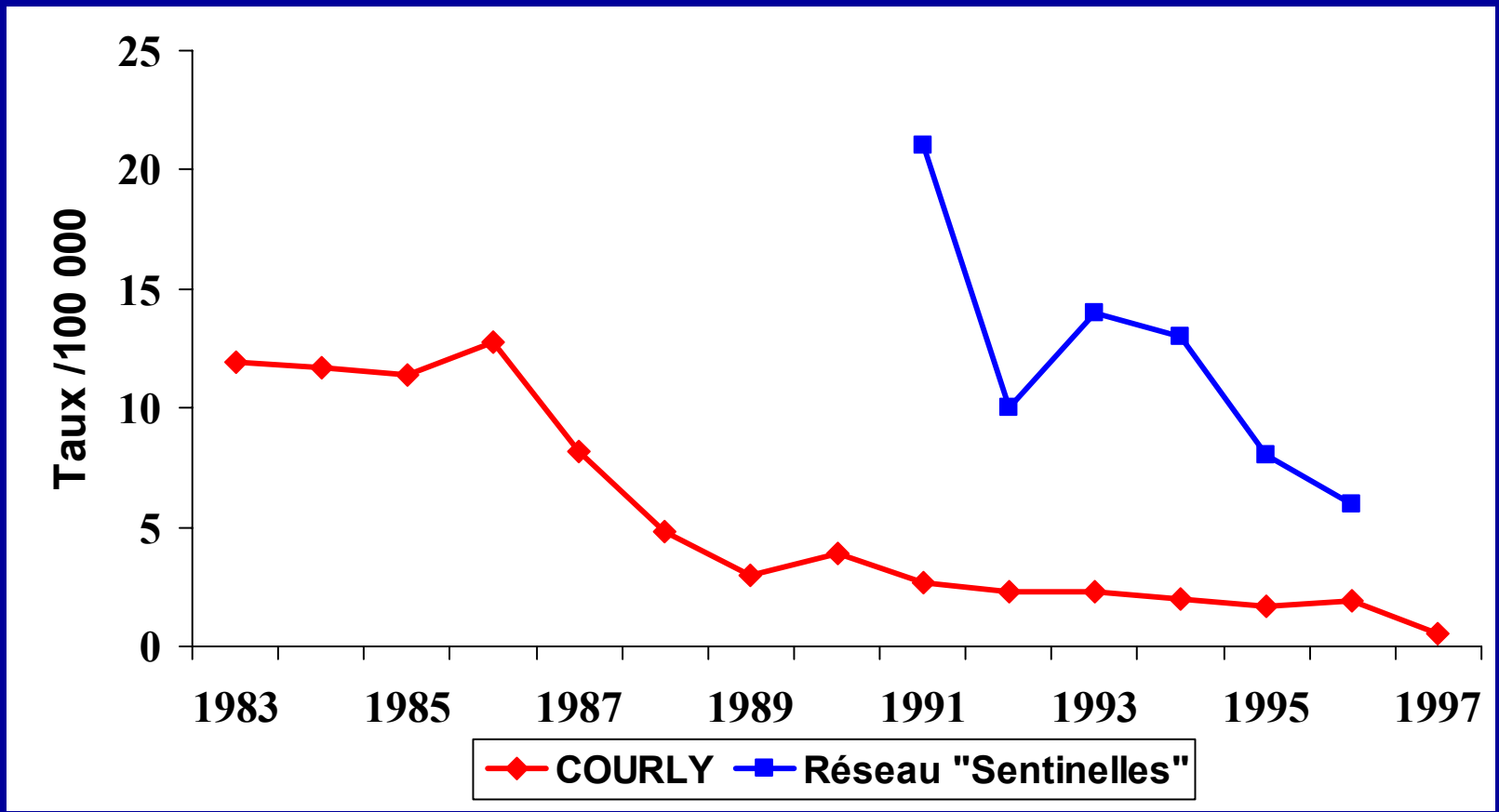
Incidence of HBV / acute hepatitis

INSTITUT DE VEILLE SANITAIRE

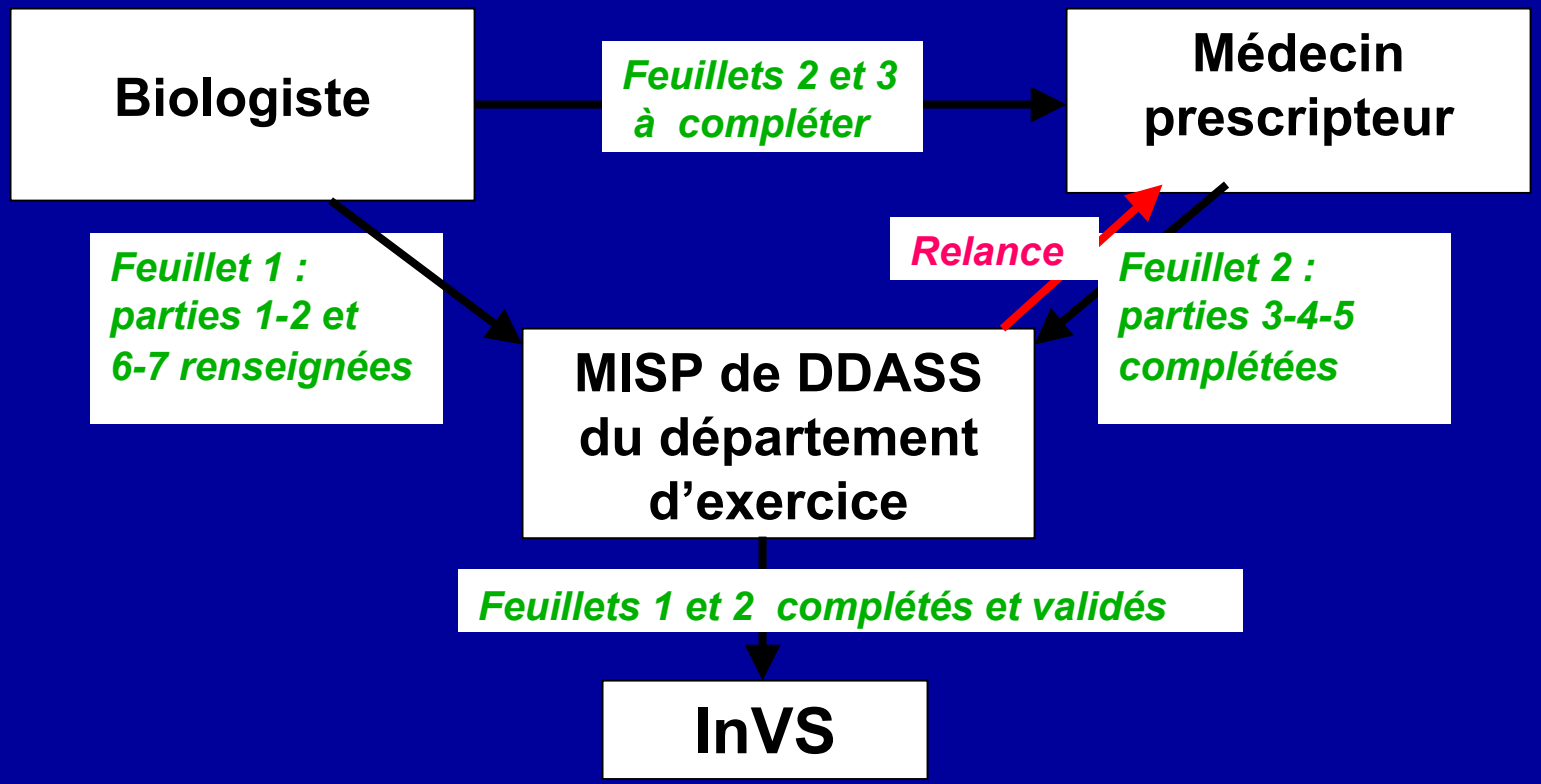
Déclaration obligatoire de l'hépatite B en France : résultats des 12 premiers mois de notification

Denise Antona, E Delarocque-Astagneau, D Lévy-Bruhl
département des maladies infectieuses

Incidence of acute hepatitis B in France
Sentinel networks 1991-1996 et Lyon (COURLY) 1983-1997



Circuit de l'information



Fiche de notification autocopiante à 4 feuillets

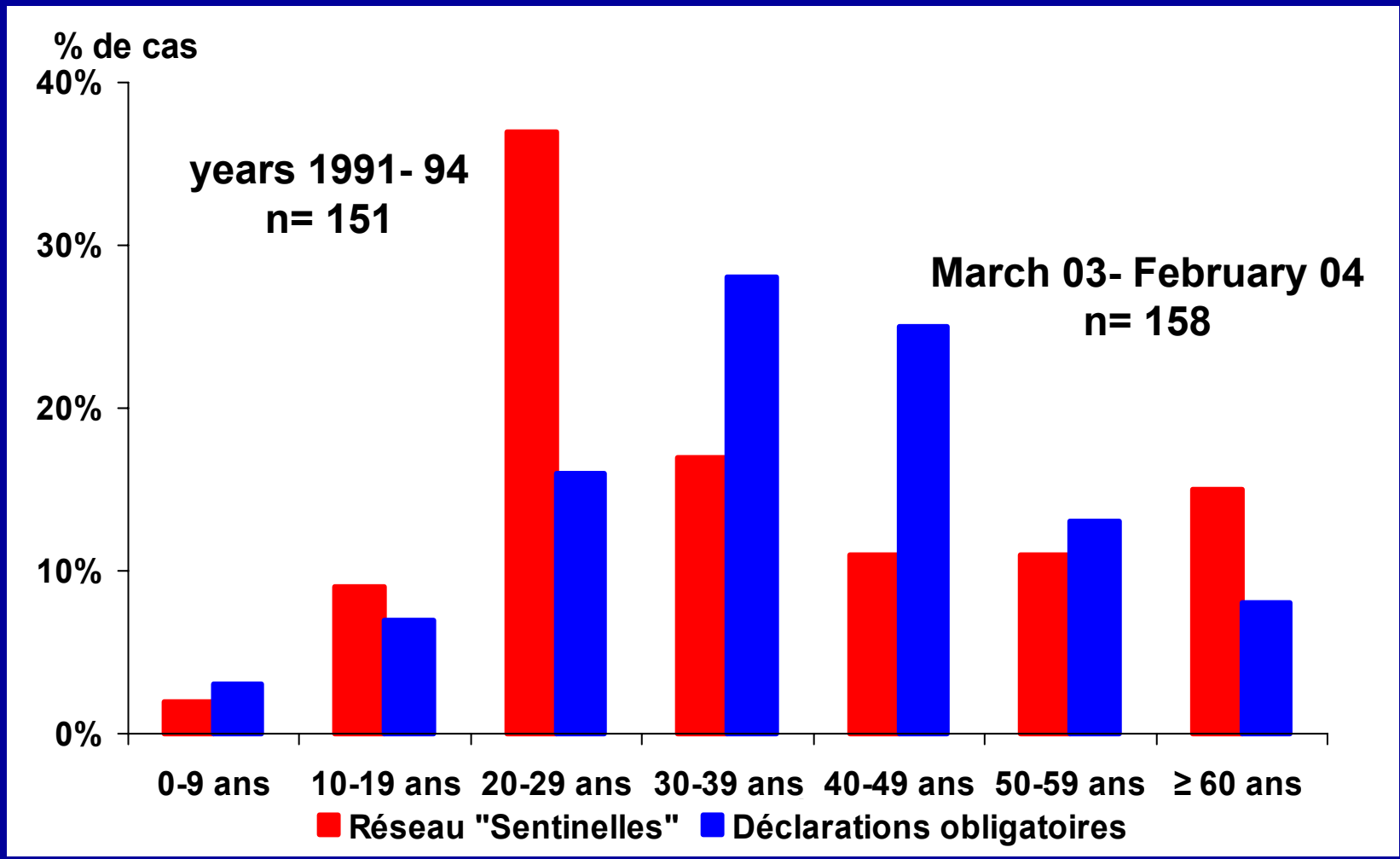
Partie 1	: code d'anonymat irréversible, caractéristiques du patient
Partie 2	: information biologique
Parties 3-4-5	: information clinique et épidémiologique
Parties 6-7	: identification du médecin prescripteur et du biologiste déclarants

Results

158 acute hepatitis cases

- **Hospital doctor in 64% cases**
- **Sex ratio M/F : 2,95 (118/40)**
- **Age median : 37 yrs for males, 36yrs for females**
- **Jaundice : 69%**
- **Hospitalisation : 46%**
- **Fulminant hepatitis : 3 (2 death)**

Age distribution: comparison of the different periods 1991-94 versus 03/2003 - 02/2004



Risk exposure within 6 months preceding the acute case
Source : obligatory declaration 2003-04

- **Source: obligatory declaration march 03- february 2004 N=145**

– Sexual	59	40,6%
– IVDU	9	6,2%
– Invasive treatment	15	10,3%
– Tatoo, piercing	5	3,4%
– Familial	14	9,7%
– Perinatal	2	1,4%
– Live in instiution	11	7,6%
– Travel in endemic areas	21	14,5%

No factor	43	29,6%
>1 factor	38	26,3%

- Sentinel networks 91-96 N=195
  - sexuael 35%
  - IVDU 19%
  - « percutaneous » 15%
  - No fzctor 35%

91/145 patients (63 %) had a vaccine indication (2 vaccinated ≥ 3 doses)

Chronic hepatitis B

THE LAMIVIR COHORT STUDY

AIMS

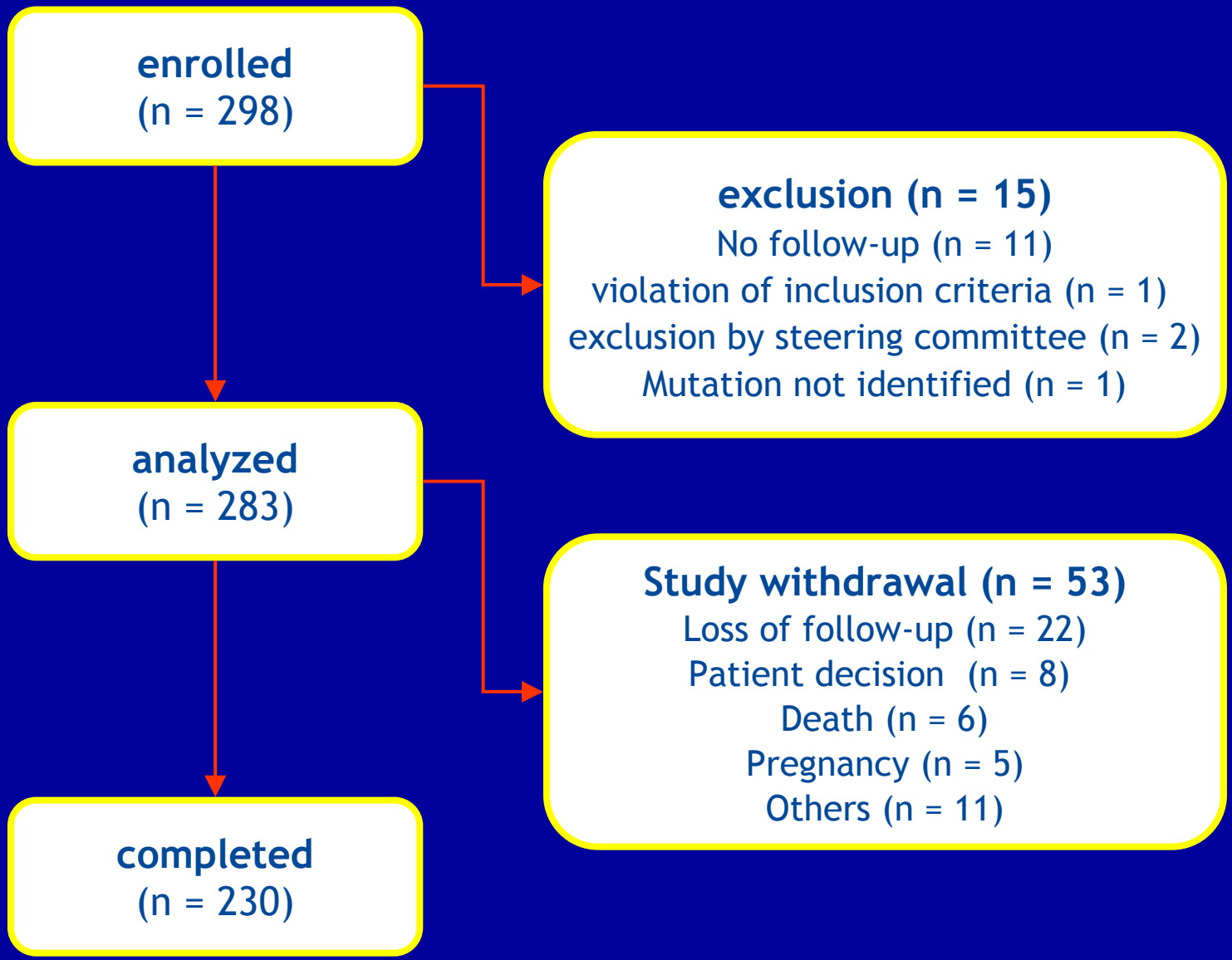
1) To study the incidence of lamivudine resistance in a daily practice setting

2) To determine the clinical severity of lamivudine resistance

3) To determine the risk factors of lamivudine resistance

Lamivir study

Patient flow



Demographic characteristics

	Serological status		TOTAL	*p*
	HBe+	HBe-		
	N = 119	N = 164	N = 283	
Age (years)				
Mean ± SD	38,6 ± 14,0	46,1 ± 12,9	42,9 ± 13,9	< 0,001
Mediane [range]	36,0 [18,0 – 82,0]	46,0 [20,0 – 83,0]	42,0 [18,0 – 83,0]	
Gender				
male	92 (77,3 %)	129 (78,7 %)	221 (78,1 %)	NS
Female	27 (22,7 %)	35 (21,3 %)	62 (21,9 %)	
BMI				
Mean ± SD	23,8 ± 4,0	24,7 ± 4,2	24,3 ± 4,1	0,036
Mediane [range]	23,2 [16,0 – 43,0]	24,1 [16,7 – 45,0]	23,7 [16,0 – 45,0]	

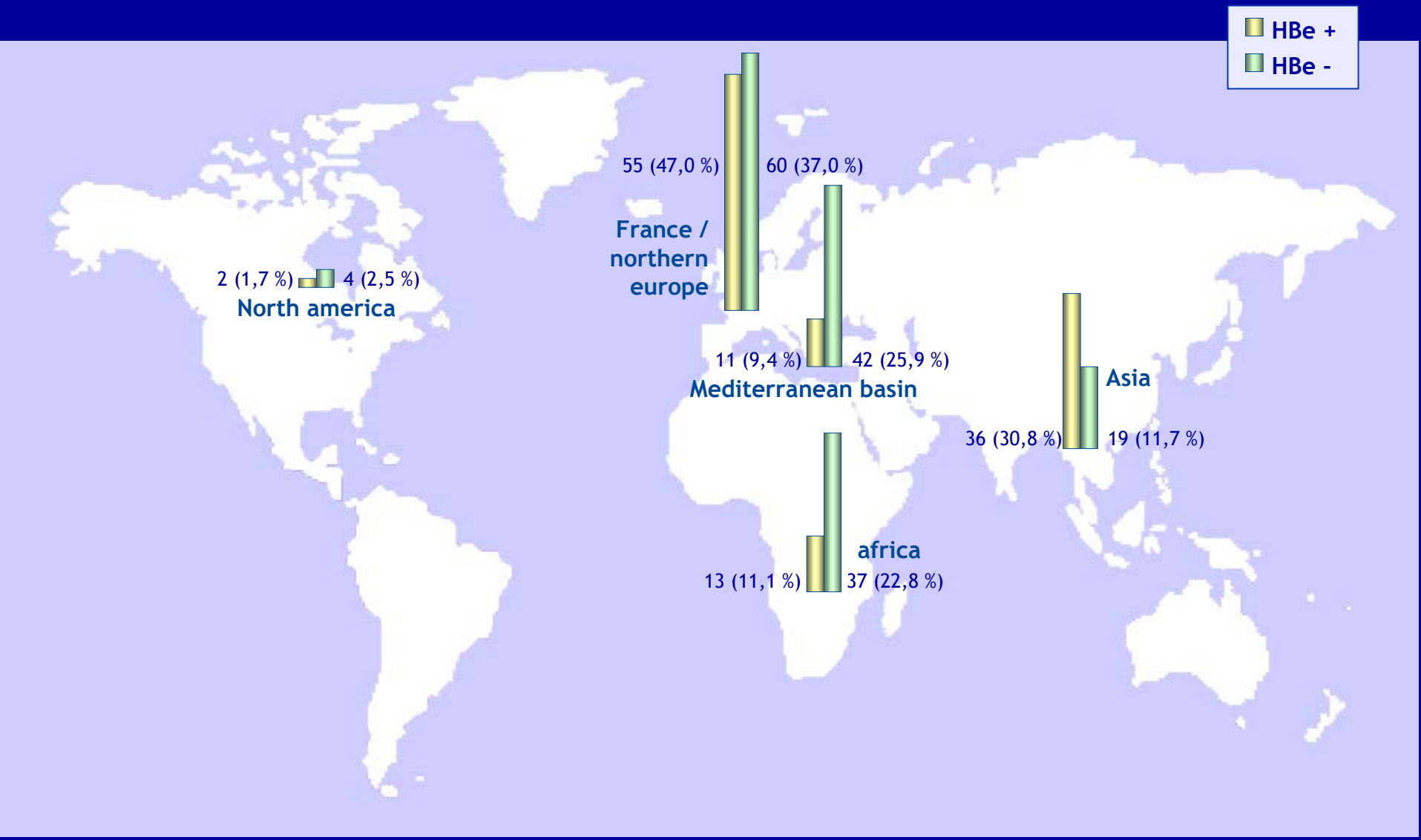
Risk Factors

	Serological status		TOTAL	*p*
	HBe+	HBe-		
	N = 119	N = 164	N = 283	
Alcohol consumption				
Regular consumption	8 (6,8 %)	21 (12,8 %)	29 (10,3 %)	NS
Daily intake (Mean ± SD)	31,3 ± 24,2	18,9 ± 15,9	22,6 ± 19,1	NS
Other risk factors				
None	14 (11,8 %)	33 (20,1 %)	47 (16,6 %)	NS
IVDU	2 (1,7 %)	1 (0,6 %)	3 (1,1 %)	NS
Sexual	17 (14,3 %)	7 (4,3 %)	24 (8,5 %)	0,003
Travel in endemia regions	49 (41,2 %)	74 (45,1 %)	123 (43,5 %)	NS
Familial transmission	40 (33,6 %)	55 (33,5 %)	95 (33,6 %)	NS
Perinatal transmission	41 (34,5 %)	42 (25,6 %)	83 (29,3 %)	NS

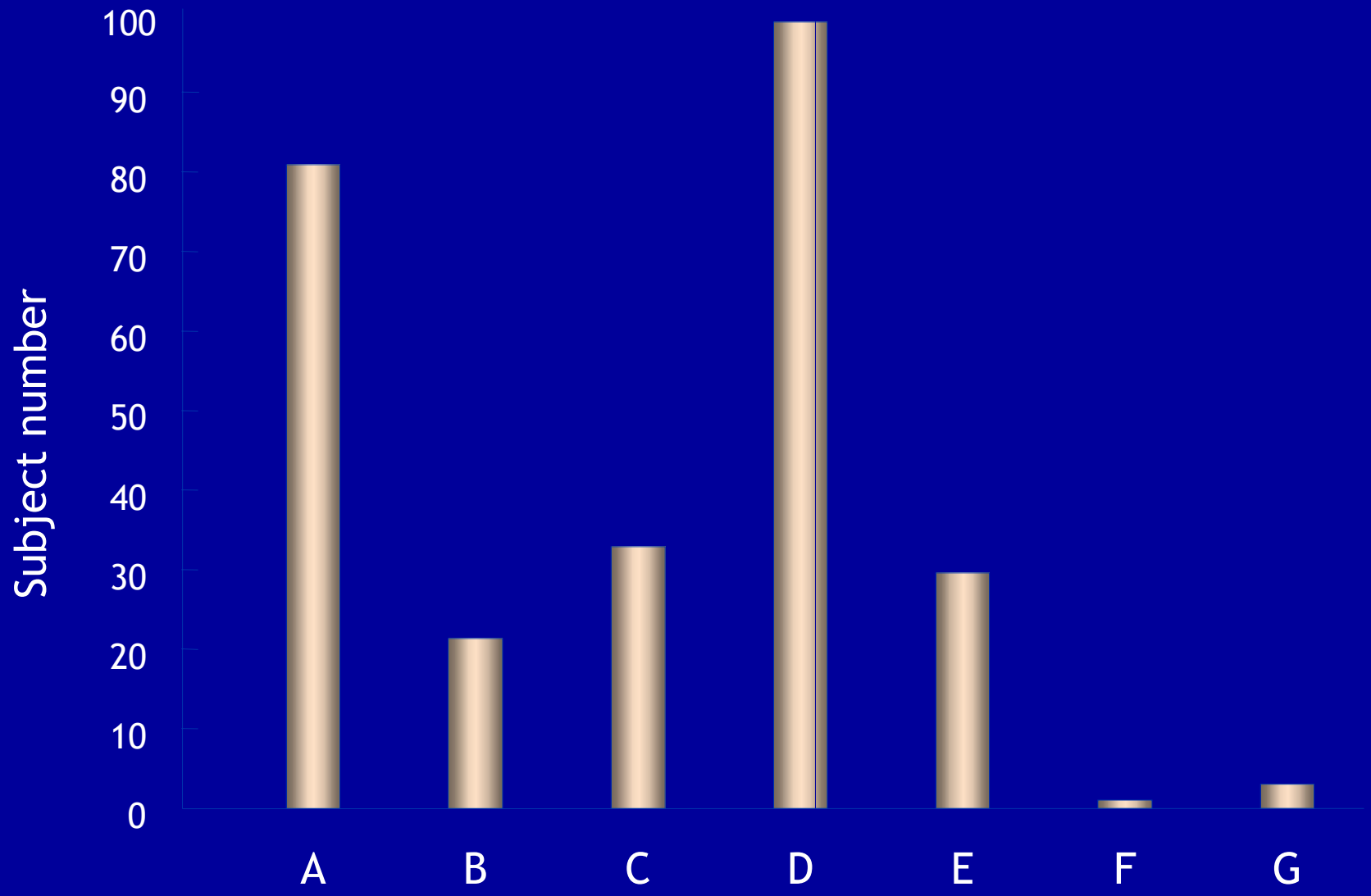
Clinical characteristics

	Serological status			*p*
	HBe+	HBe-		
	N = 119	N = 164	N = 283	
Disease duration (years)				
Mean ± SD	5,8 ± 6,0	6,7 ± 7,5	6,3 ± 6,9	NS
Mediane [range]	4,3 [0,1 – 30,8]	3,8 [0,1 – 41,7]	4,0 [0,1 – 41,7]	
Symptoms				
Asthenia	41 (34,5 %)	75 (45,7%)	116 (41,0 %)	NS
Anorexia	9 (7,6 %)	7 (4,3%)	16 (5,7 %)	NS
Weight loss	6 (5,0 %)	11 (6,7%)	17 (6,0 %)	NS
Jaundice	3 (2,5 %)	5 (3,0 %)	8 (2,8 %)	NS
Hepatomegaly	6 (5,0 %)	18 (11,0 %)	24 (8,5 %)	NS
Ascitis	3 (2,5%)	3 (1,8 %)	6 (2,1 %)	NS
Portal Hypertension	5 (4,2%)	10 (6,1 %)	15 (5,3 %)	NS
Ohter viral infections				
HCV	0 (0,0 %)	1 (0,6 %)	1 (0,4 %)	NS
HDV	2 (1,7 %)	1 (0,6 %)	3 (1,1 %)	NS

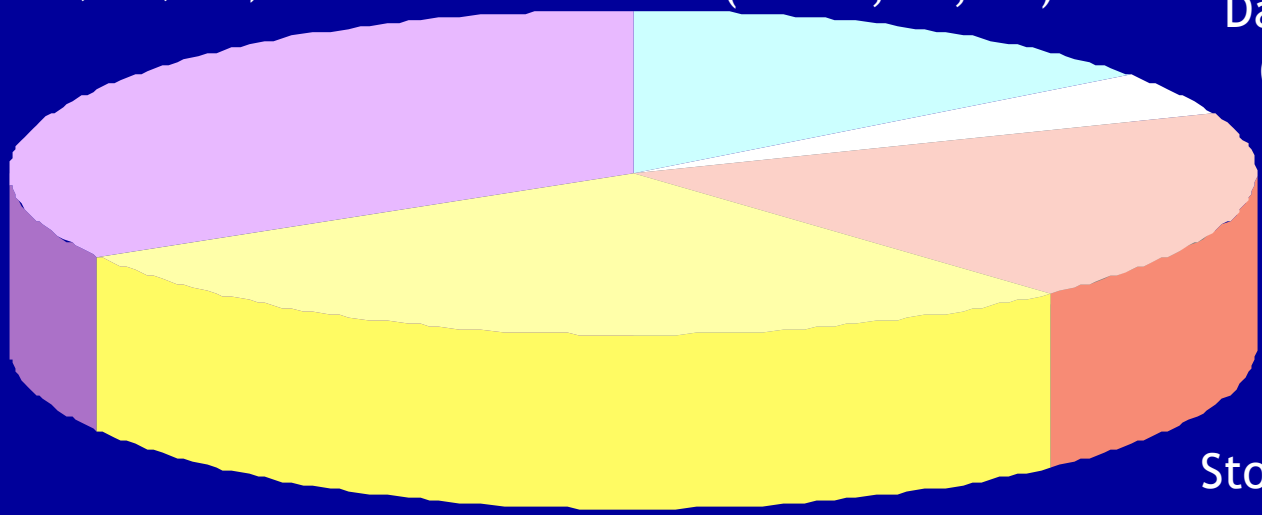
Place of Birth



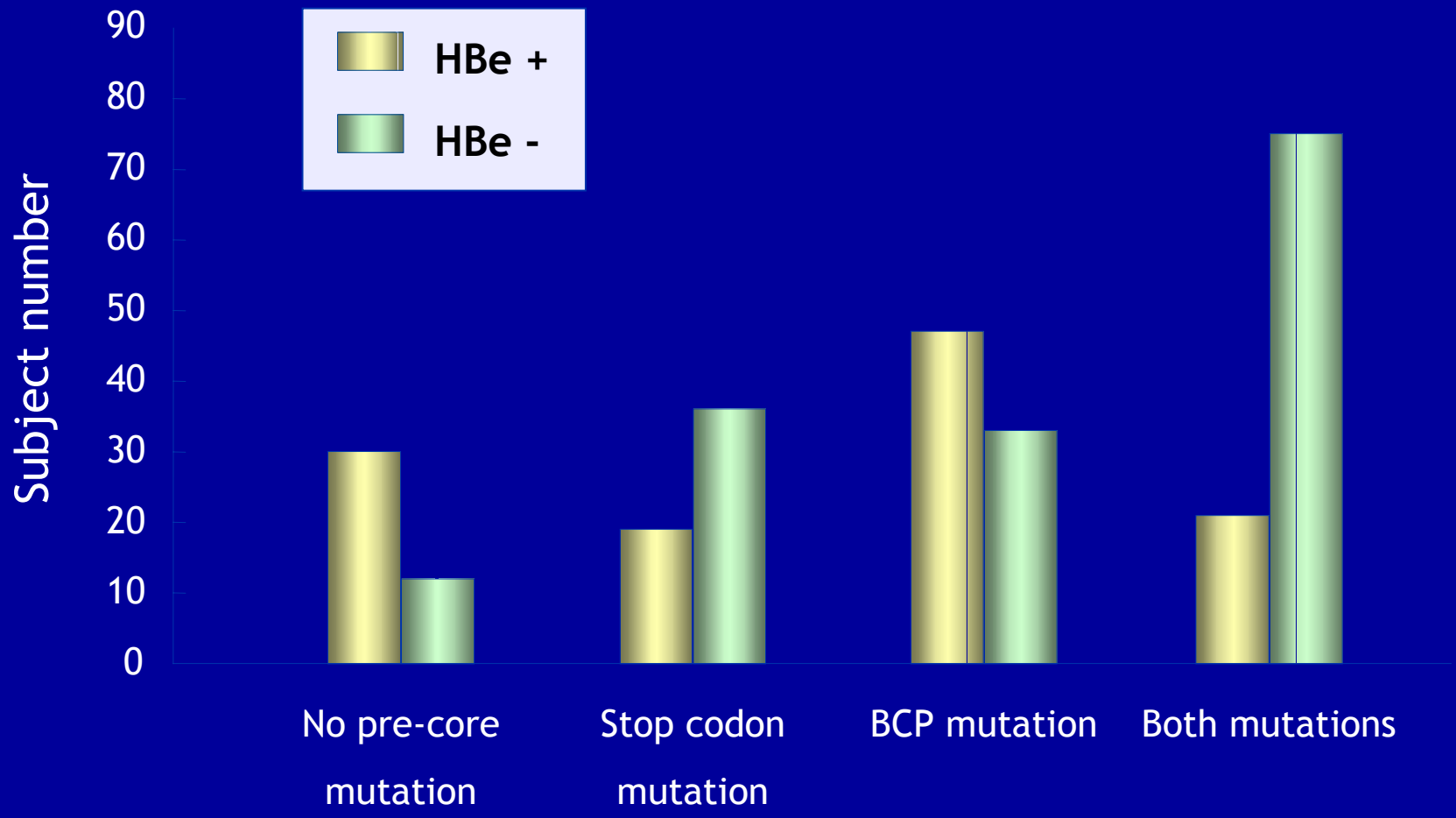
HBV genotype distribution



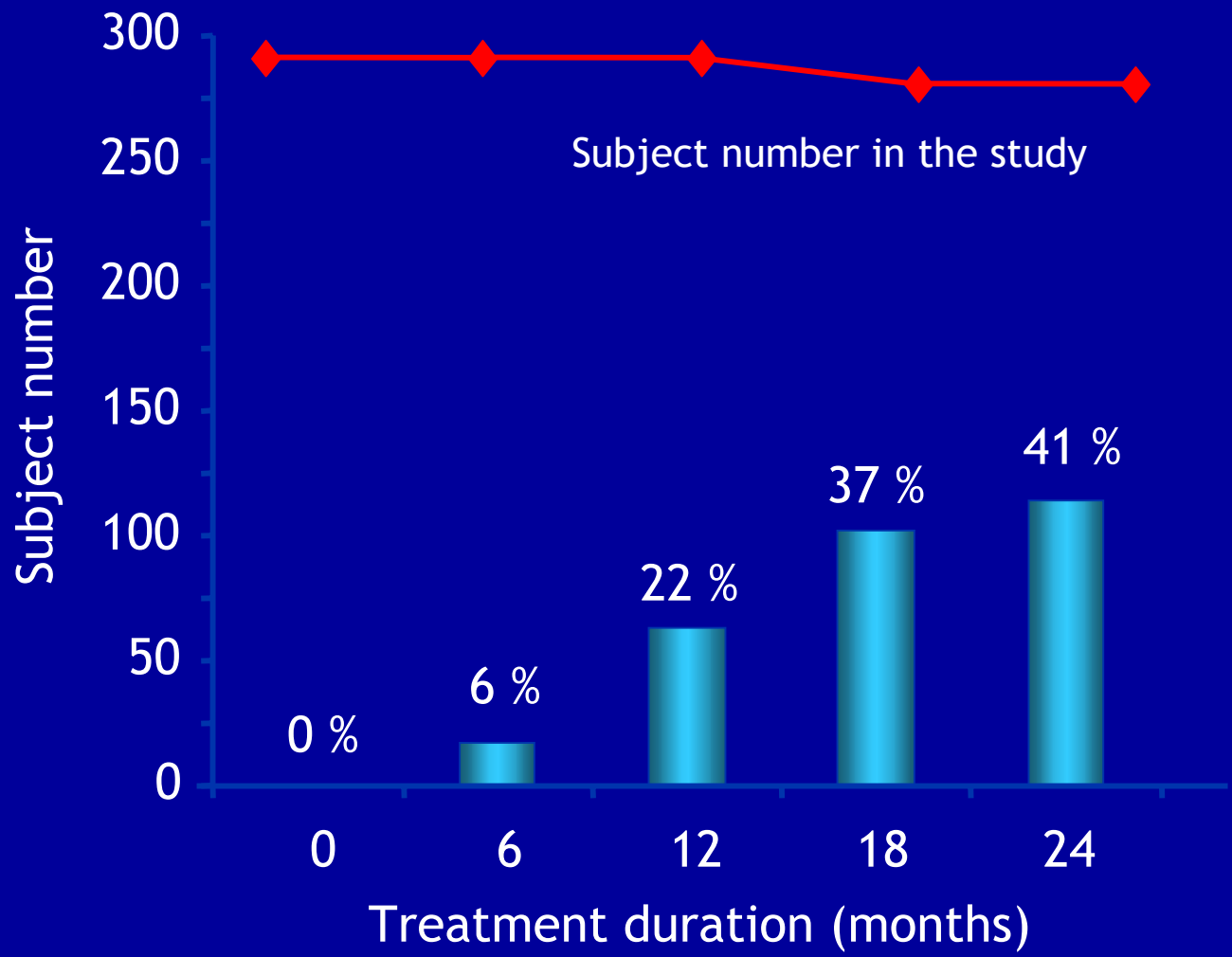
Distribution of pre-core mutants



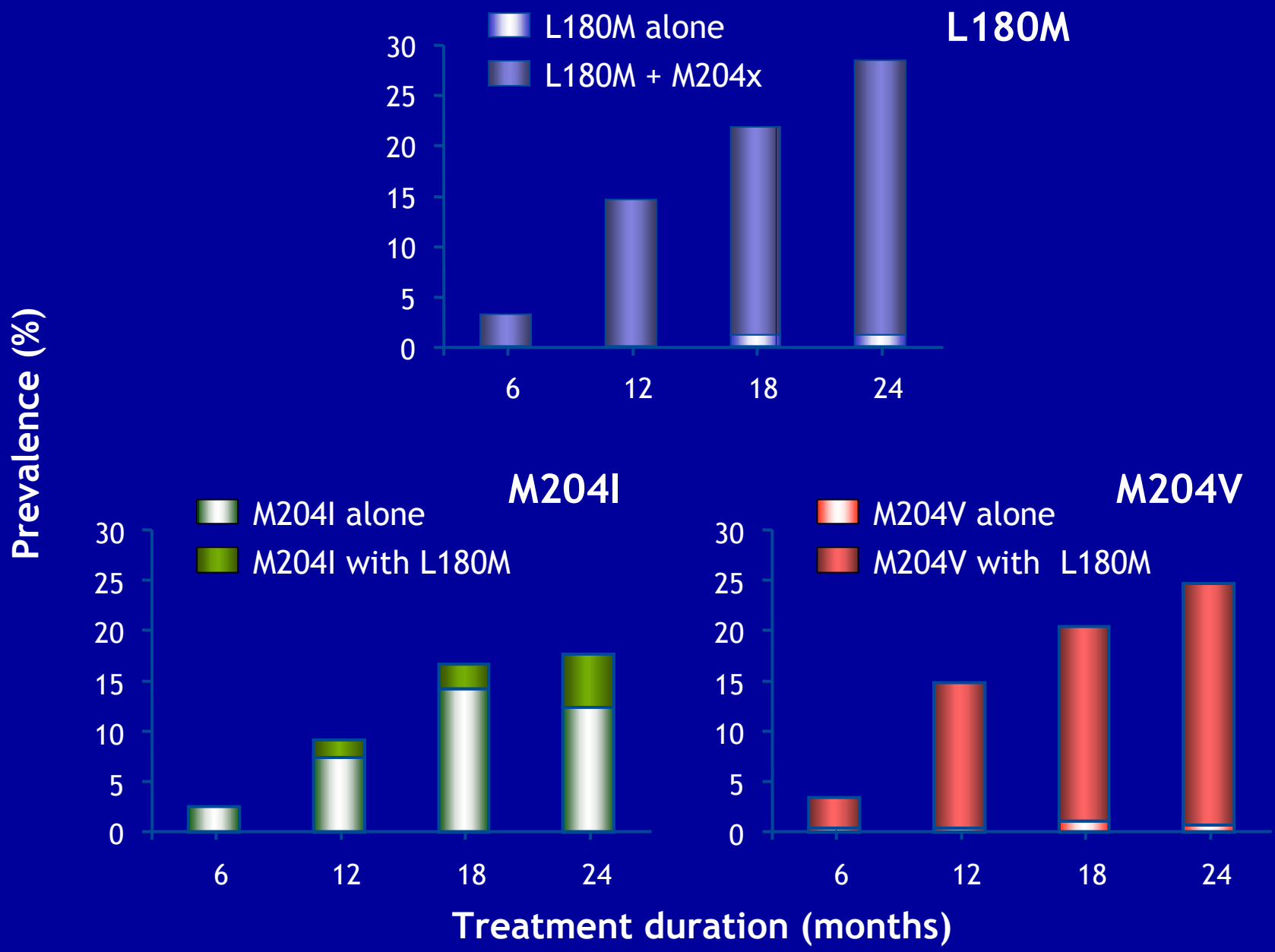
HBe status and pre-core mutants



Emergence of lamivudine resistance mutations



Distribution of polymerase mutations



Factors associated with the detection of lamivudine resitant mutants

Multivariate analysis

Baseline viral load is the only independent factor associated with the subsequent development of lamivudine resistance

Odds ratio : 1,94 [1,07 - 3,50]

(superior to versus inferior to à 5 x 10^6)

Viral load	YMDD -	YMDD +
mean (copies/ml)	7,7 x 10^6	9,8 x 10^6
mediane (copies/ml)	3,2 x 10^6	11,7 x 10^6

Conclusions

-> Prevention and vaccine

-> Improve the epidemiological studies of HBV infection

- 61% of acute cases could have been prevented by vaccination
- Problem of drug resistance in chronic hepatitis B patients
- Reinforce prevention strategies in new-borns
- Enhance prophylaxis actions
- Improve the obligatory declaration system

ACKNOWLEDGEMENTS

- **Acute hepatitis B**
  - **Dr Antona, Dr Delarocque-Astagneau, Dr Lévy-Bruhl**
  - **INVS**
- **Chronic Hepatitis B**
  - **Lamivir cohort investigators**
  - **INSERM U271 collaborators**