

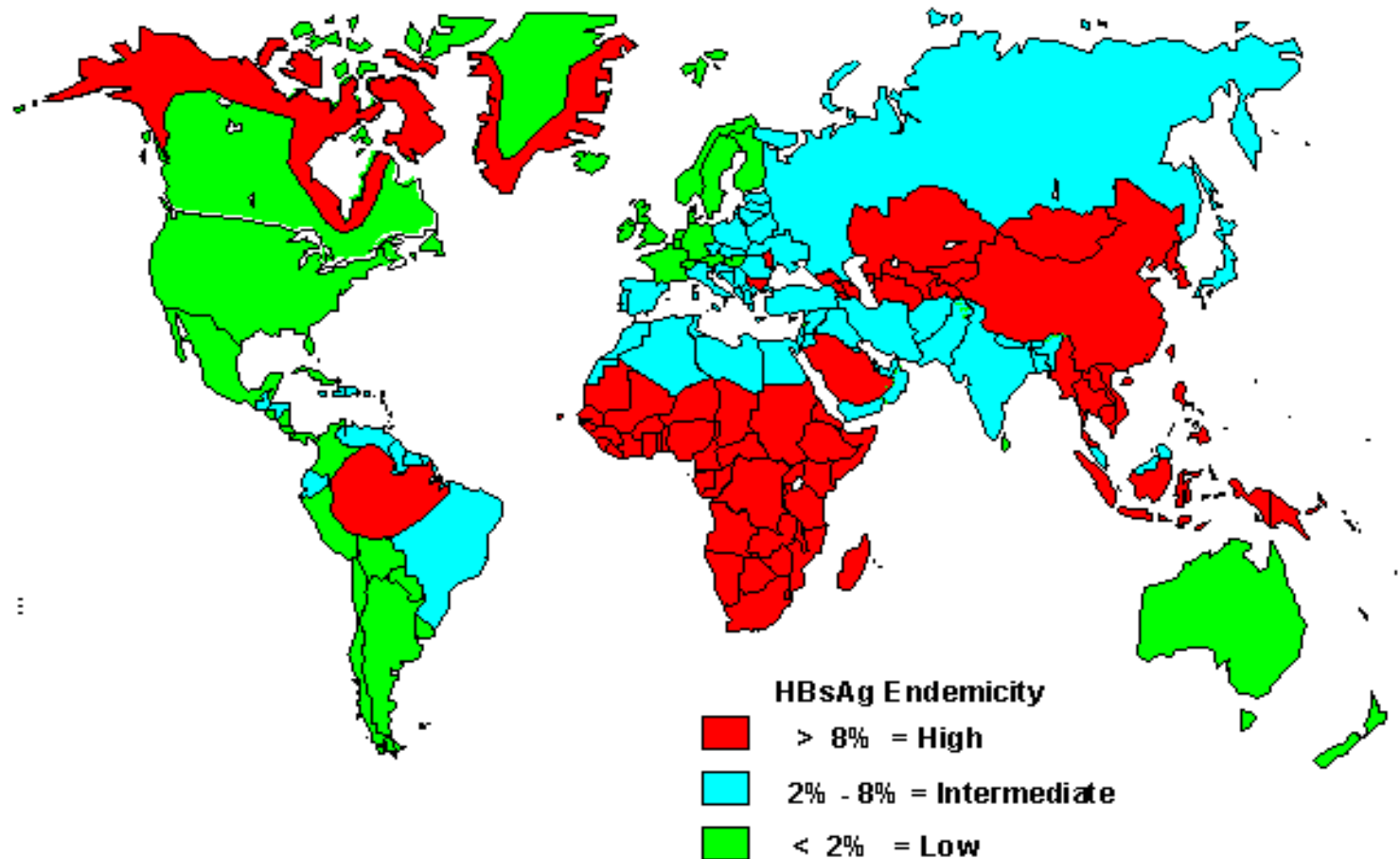
Epidemiology of HBV in France

Fabien Zoulim

Liver department & INSERM U271

Lyon, France

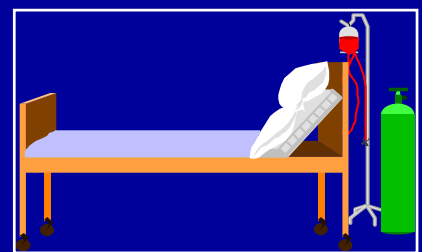
Geographic Pattern of Hepatitis B Prevalence, 1997



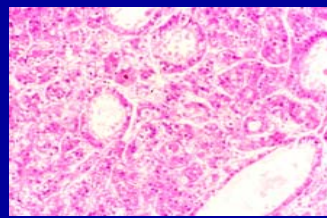
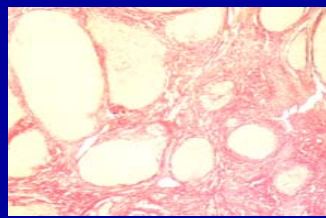
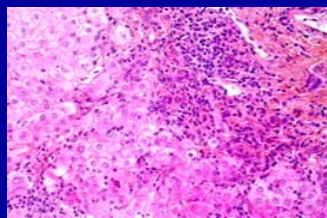
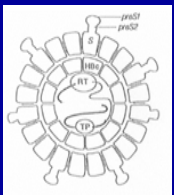
Data as of 06/04/98



Resolution



30-50 yrs



HBV



CAH



cirrhosis



HCC



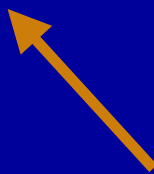
Vaccine



**ANTIVIRALS
IFN**



IFN?



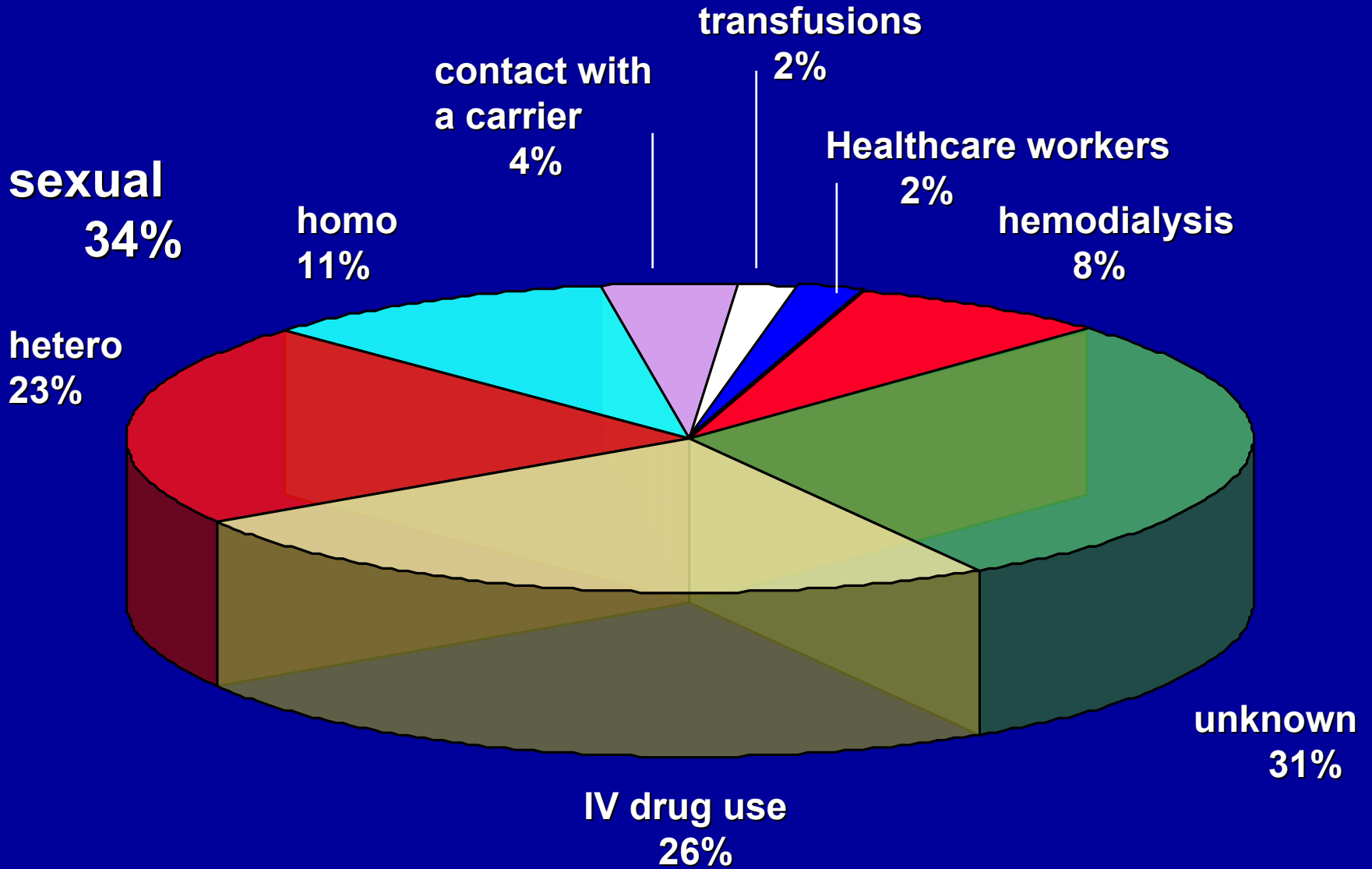
VIRAL RESISTANCE/ESCAPE

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



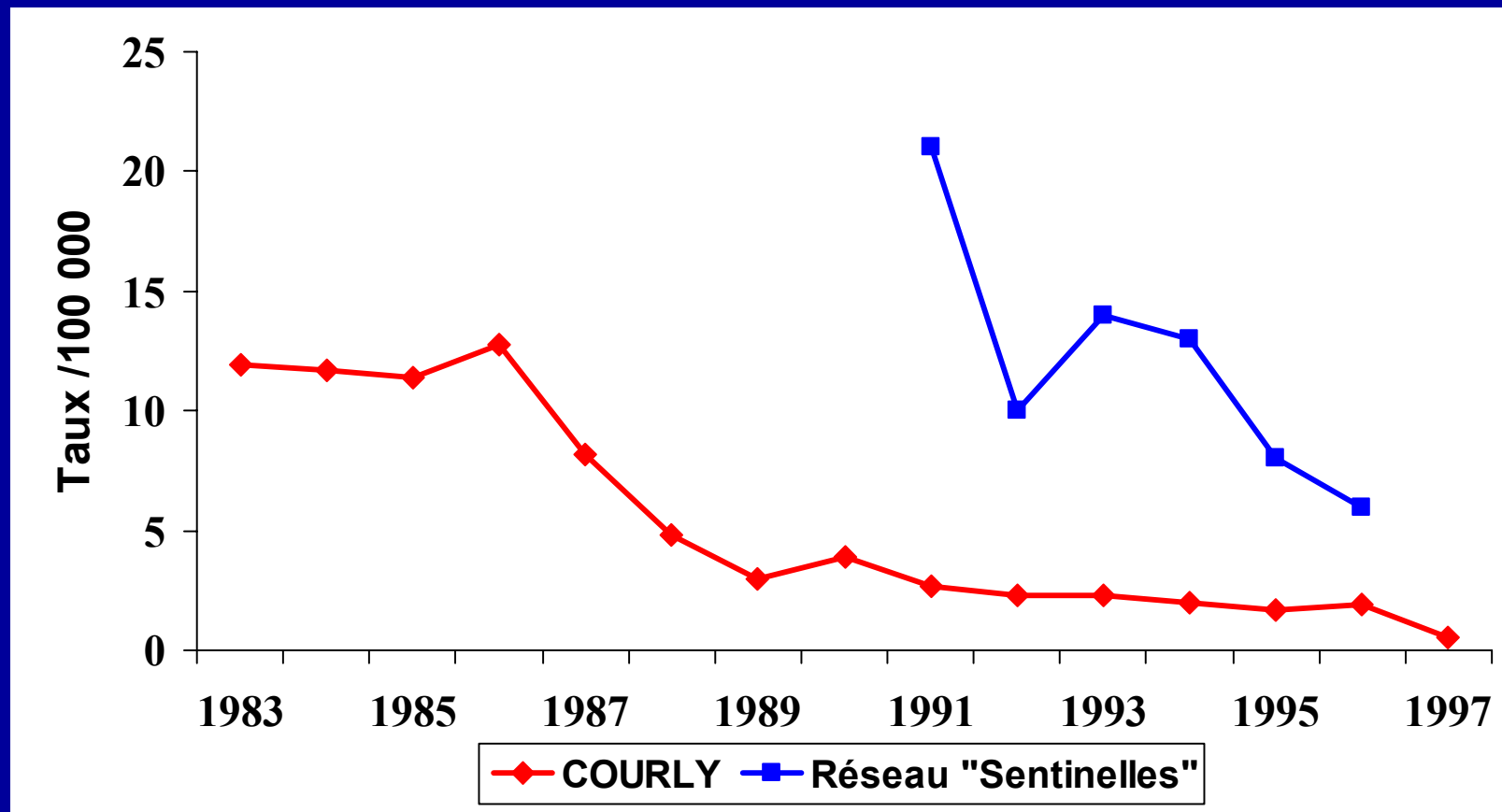
INSTITUT DE
VEILLE SANITAIRE

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

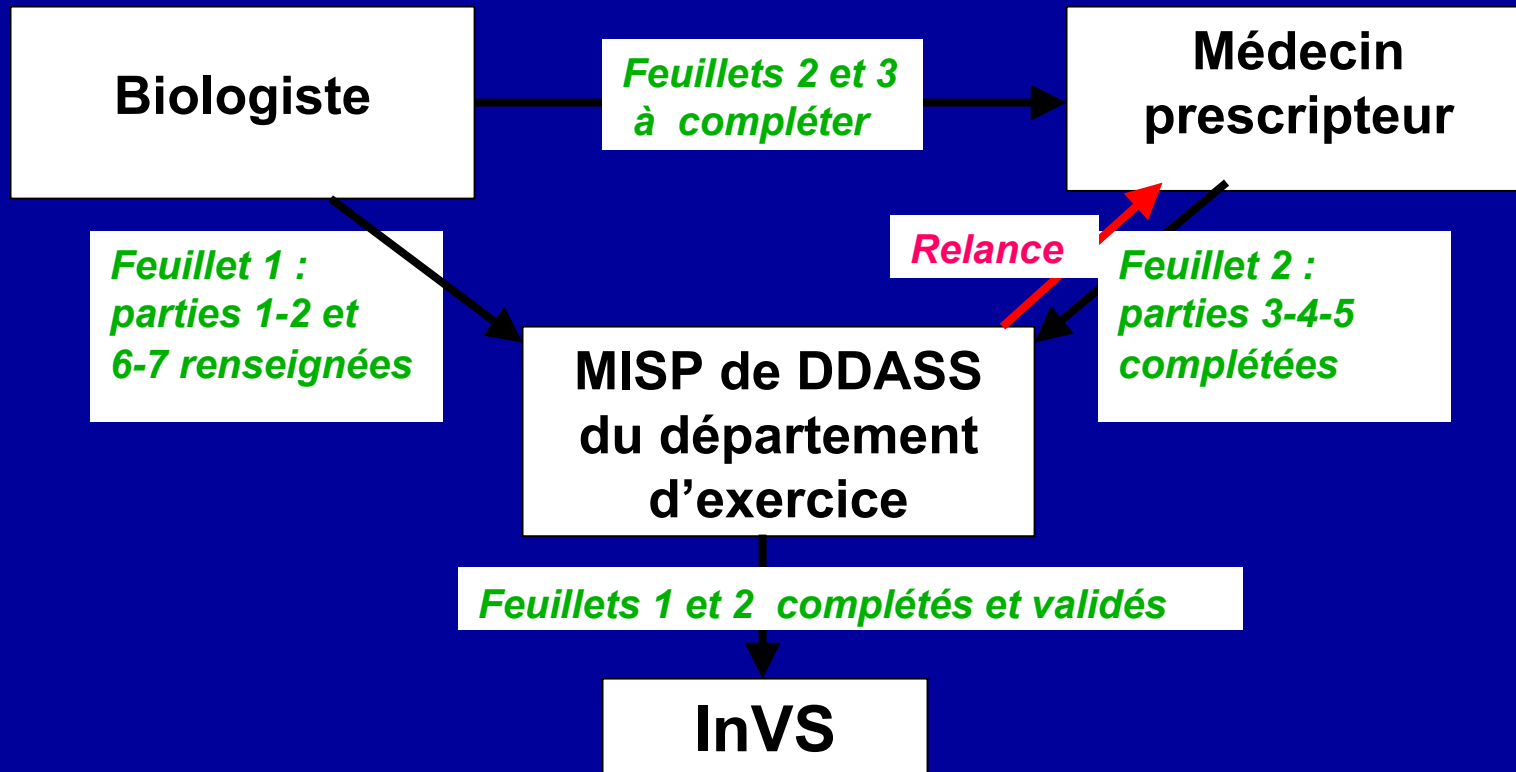
**Denise Antona, E Delarocque-Astagneau, D Lévy-Bruhl
département des maladies infectieuses**

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

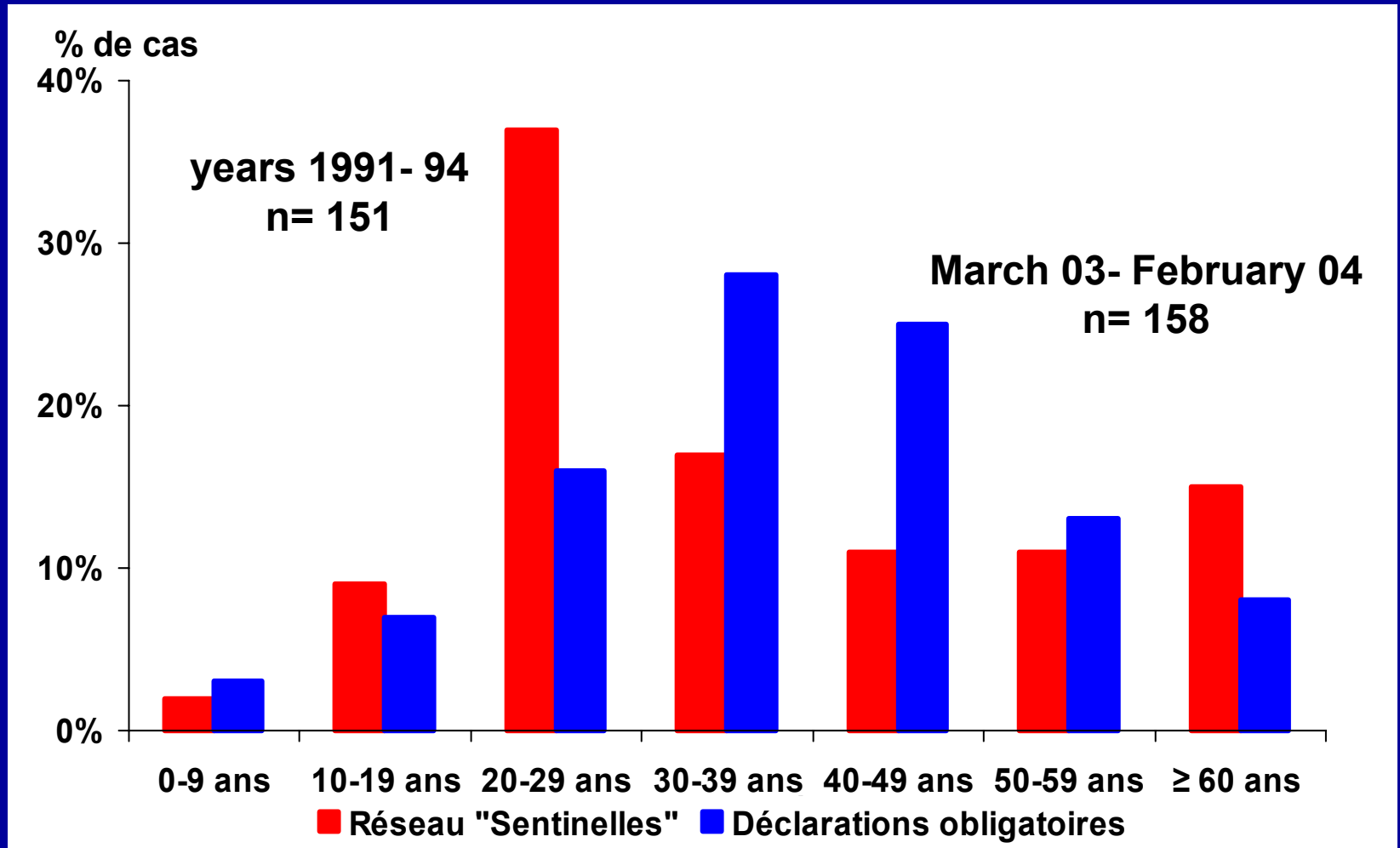
Parties 6-7 : identification du médecin prescripteur et du biologiste déclarants

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%	No factor	43	29,6%
– IVDU	9	6,2%	>1 factor	38	26,3%
– Invasive treatment	15	10,3%			
– Tadoo, piercing	5	3,4%			
– Familial	14	9,7%			
– Perinatal	2	1,4%			
– Live in instiution	11	7,6%			
– Travel in endemic	21	14,5%			

areas

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

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

Chronic hepatitis B

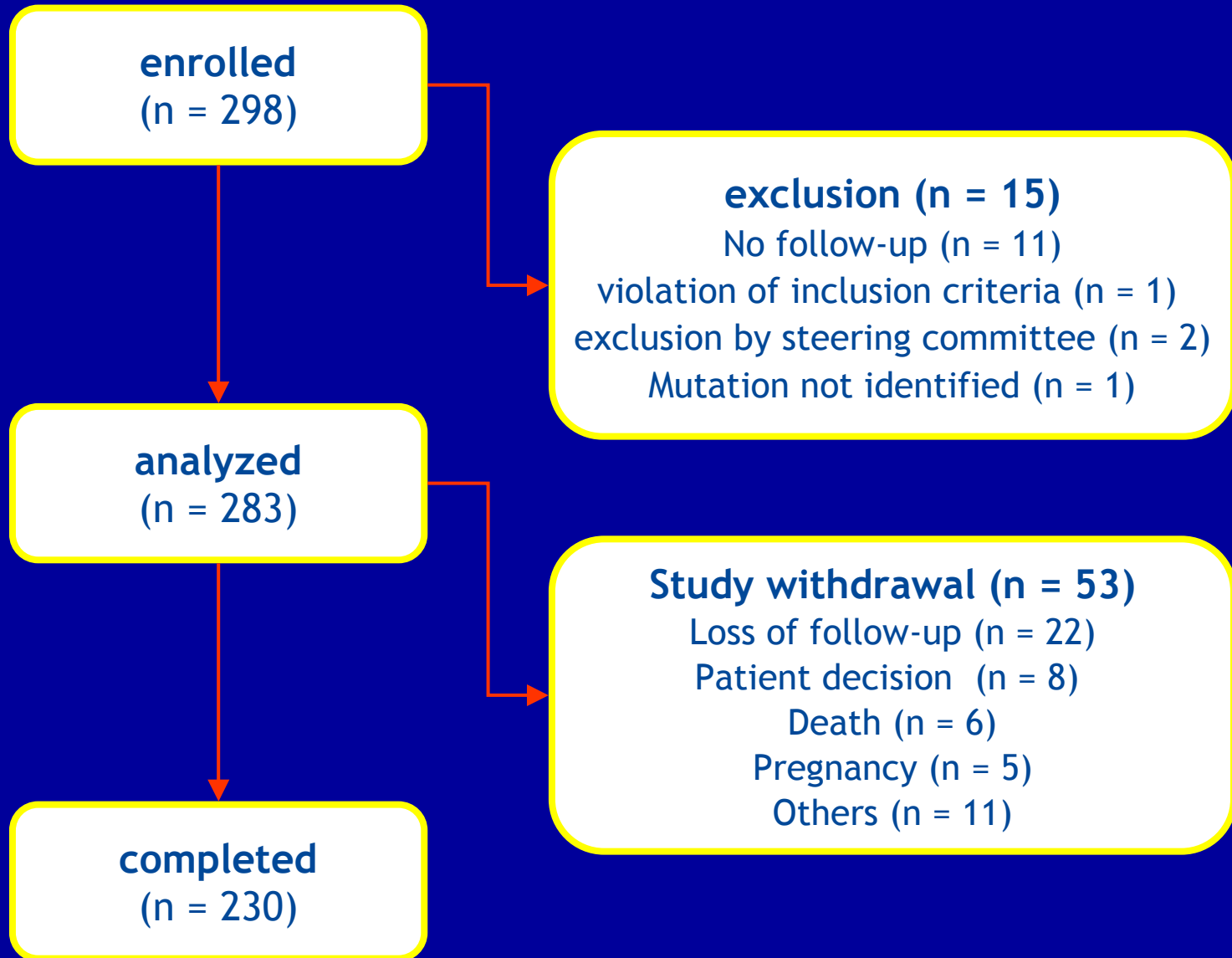
THE LAMIVIR COHORT STUDY

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]	

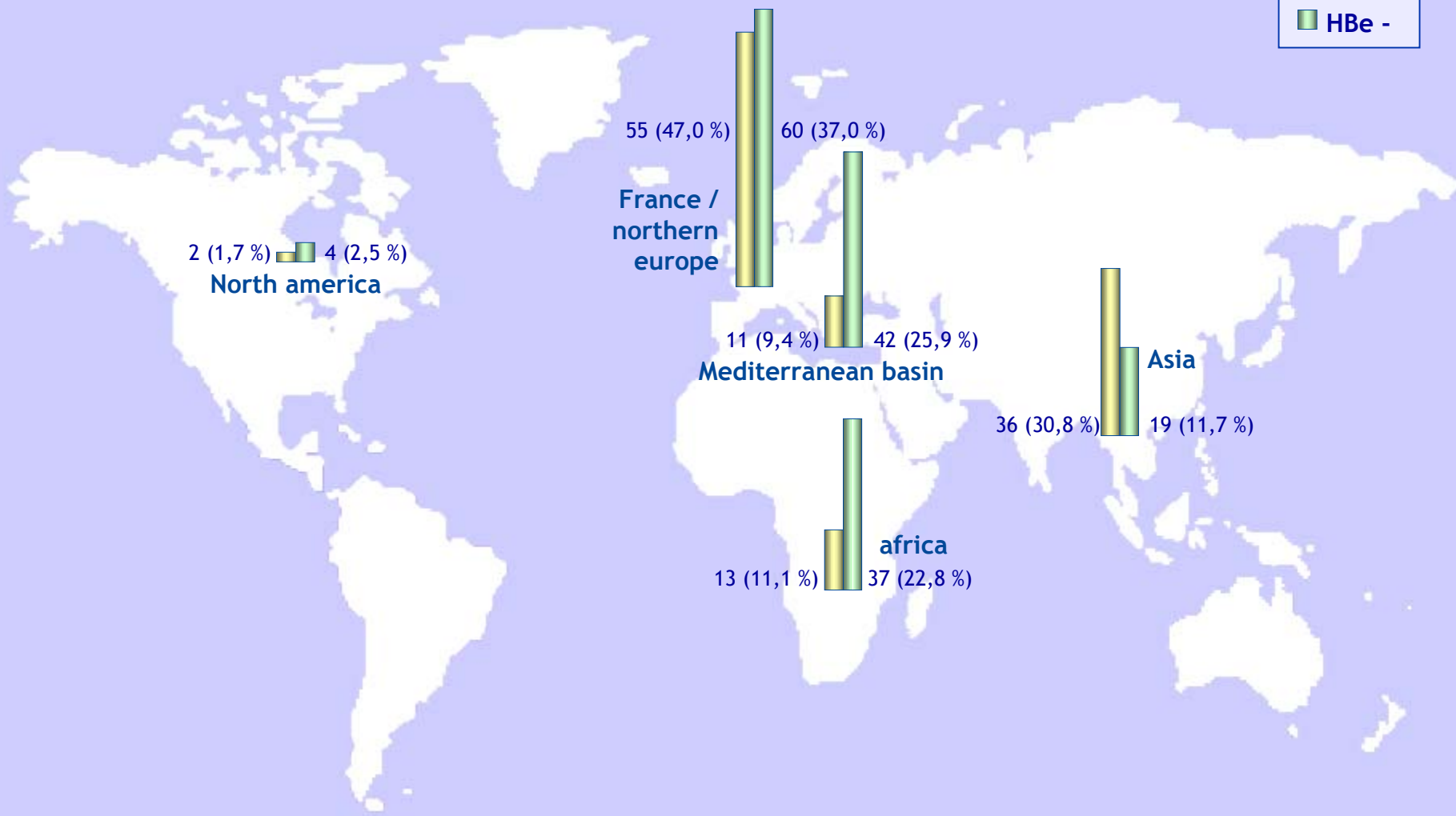
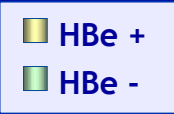
Risk Factors

	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

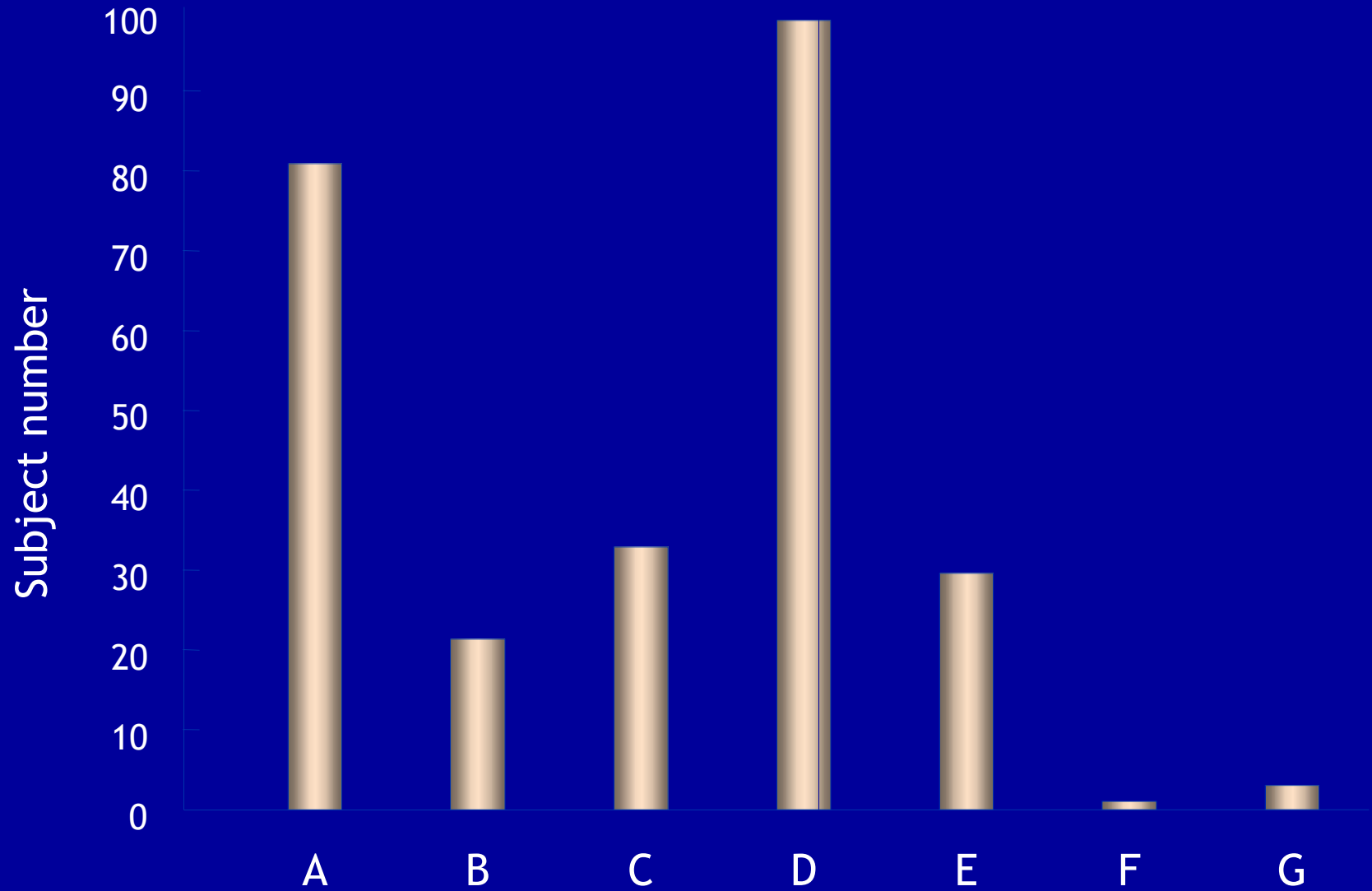
Clinical characteristics

	Serological status		N = 283	p
	HBe+	HBe-		
	N = 119	N = 164		
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

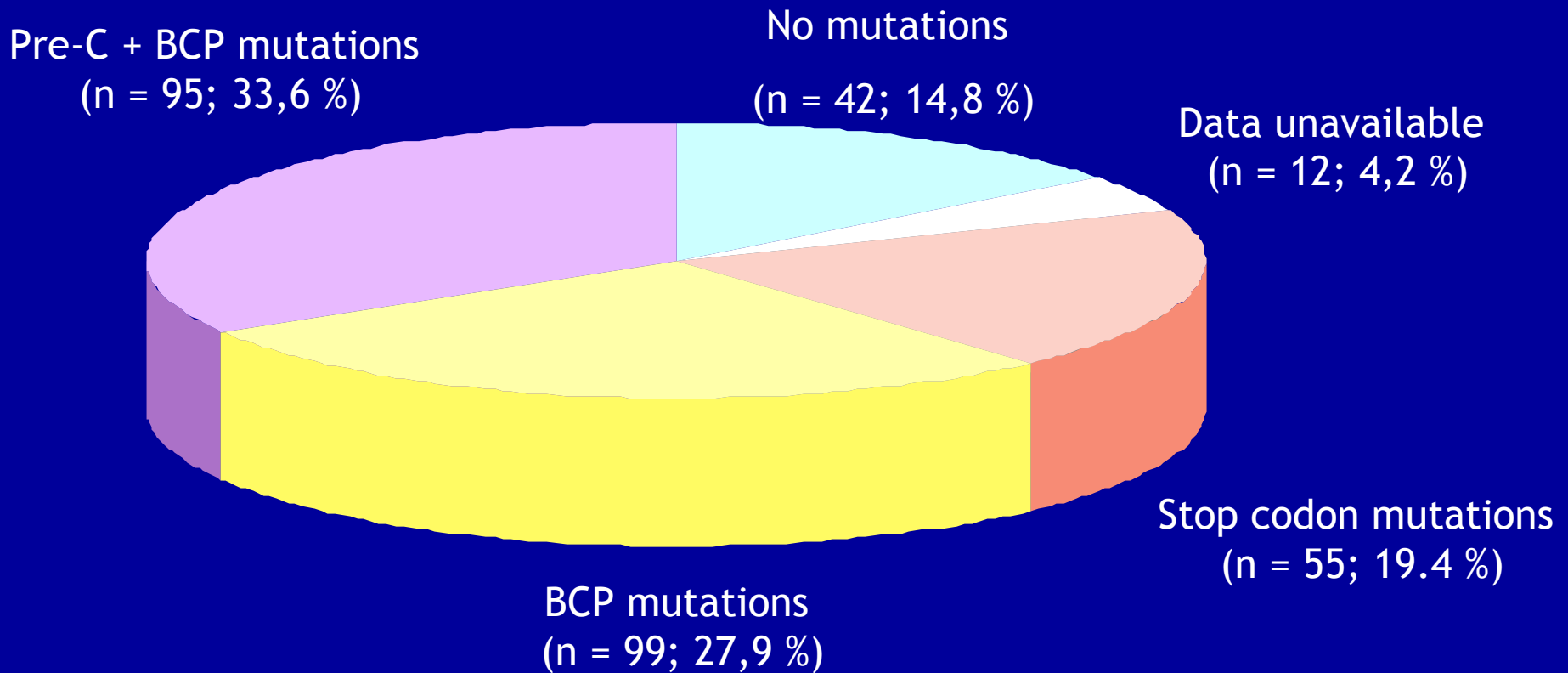
Place of Birth



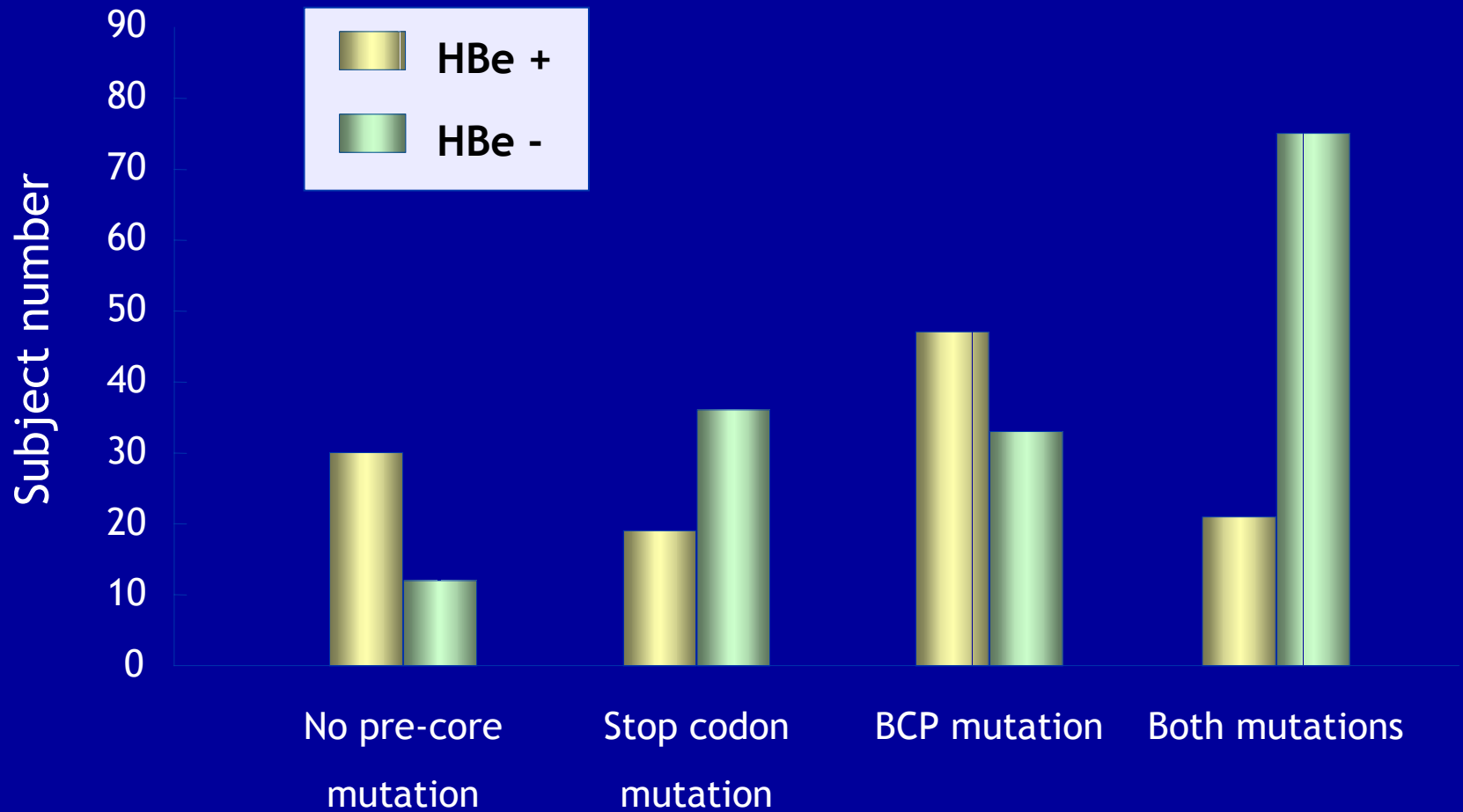
HBV genotype distribution



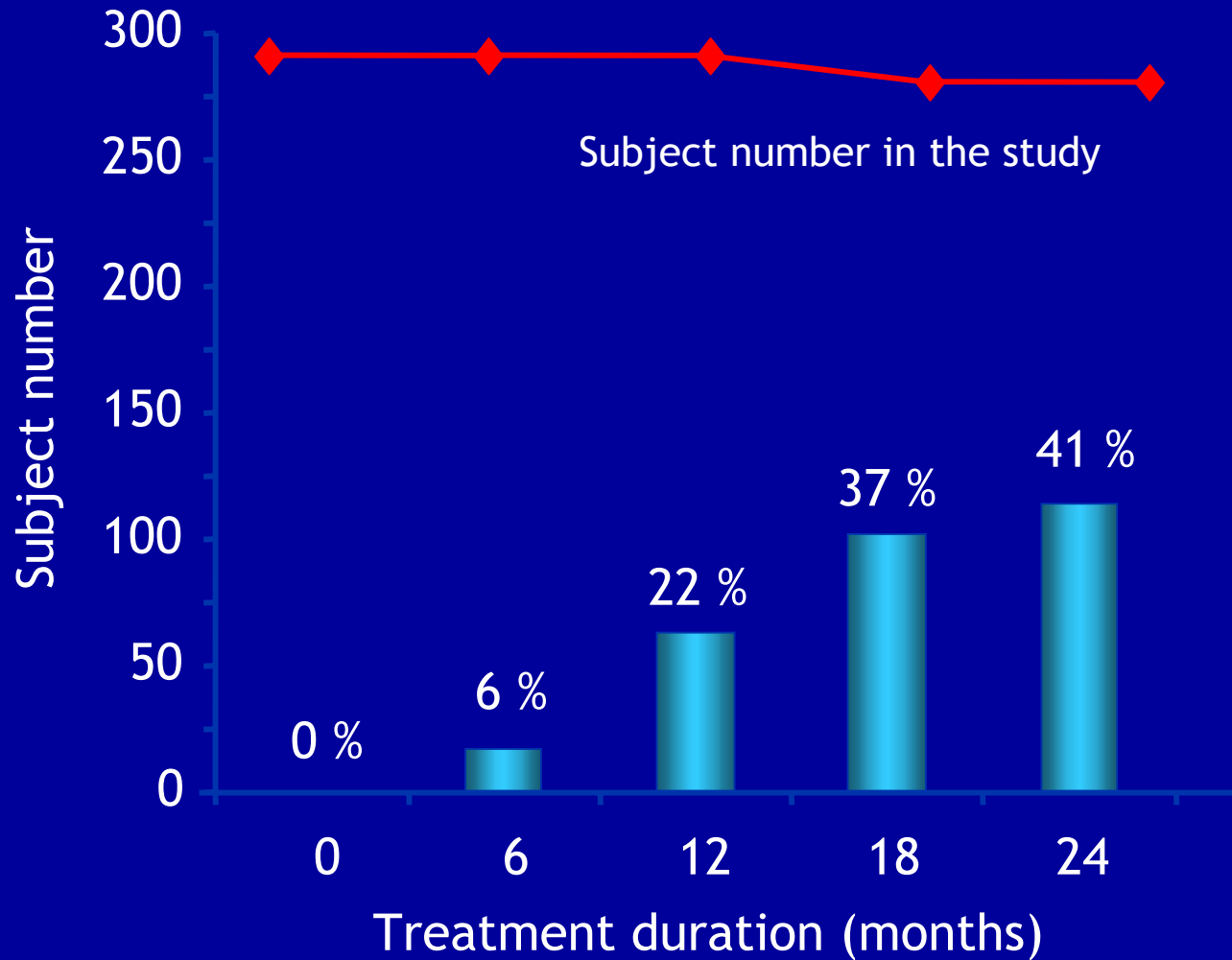
Distribution of pre-core mutants



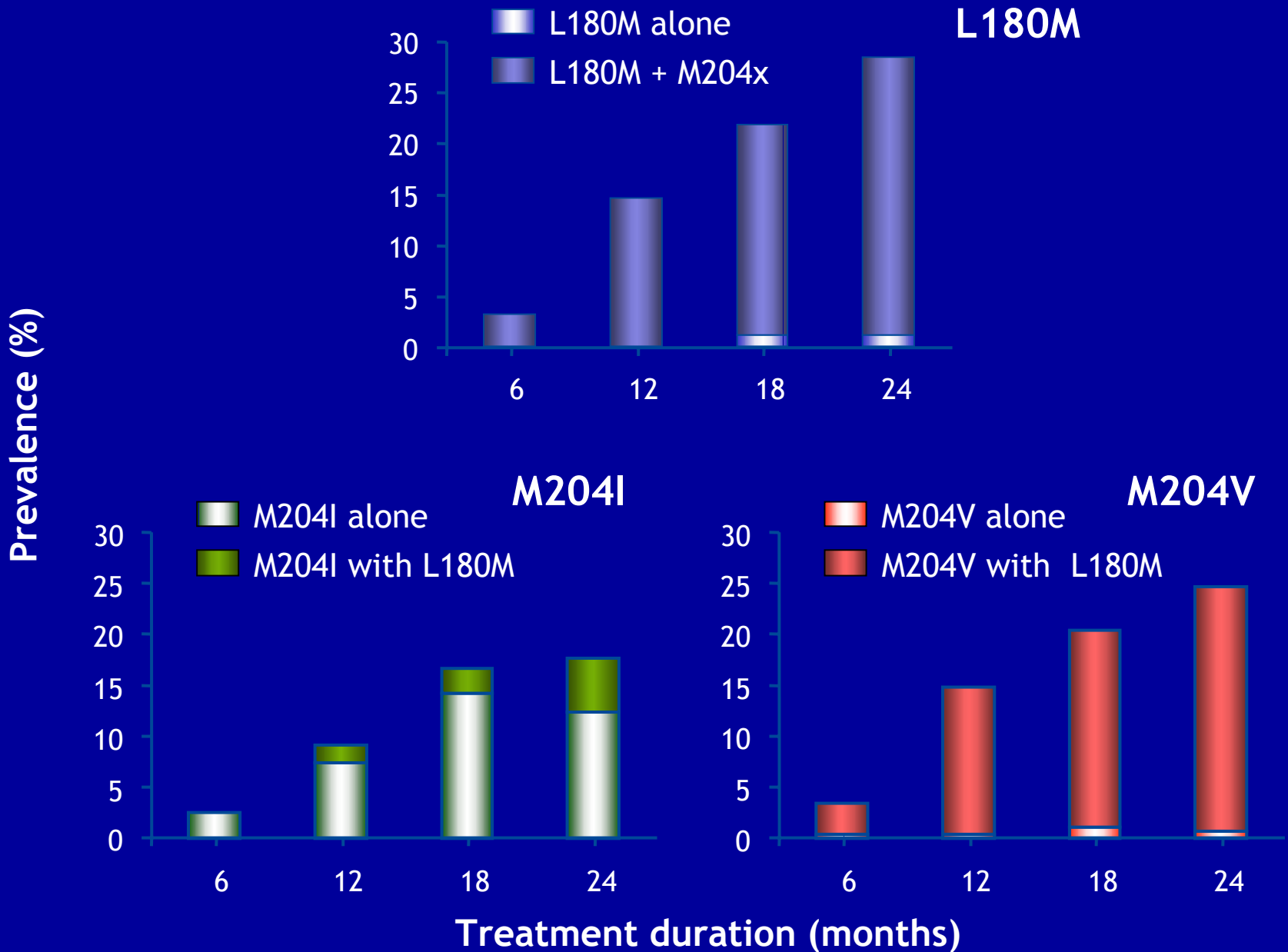
HBe status and pre-core mutants



Emergence of lamivudine resistance mutations



Distribution of polymerase mutations



Factors associated with the detection of lamivudine resistant 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 5×10^6)

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

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