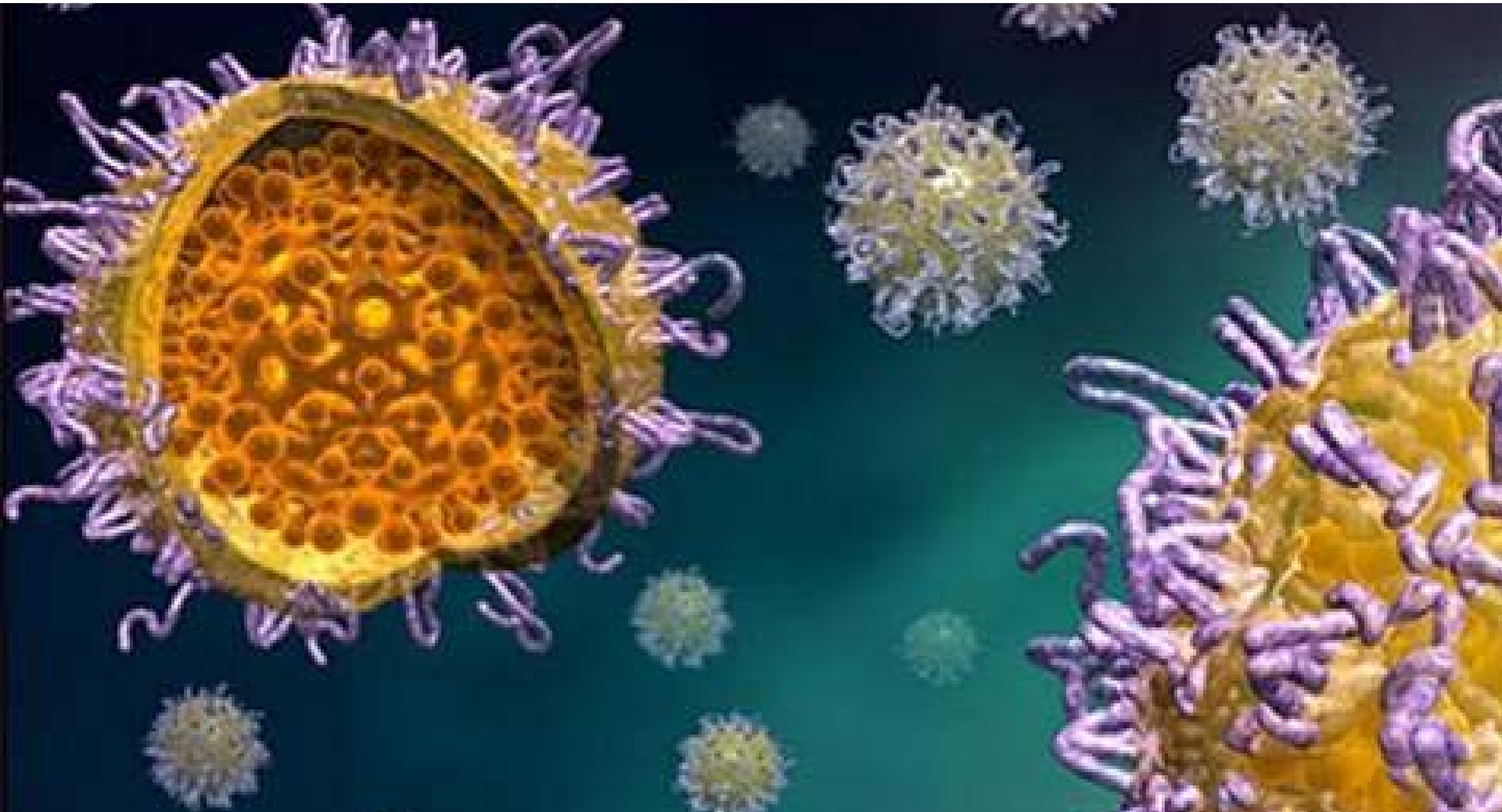


Molecular epidemiology of HBV in The Netherlands

Hein J. Boot



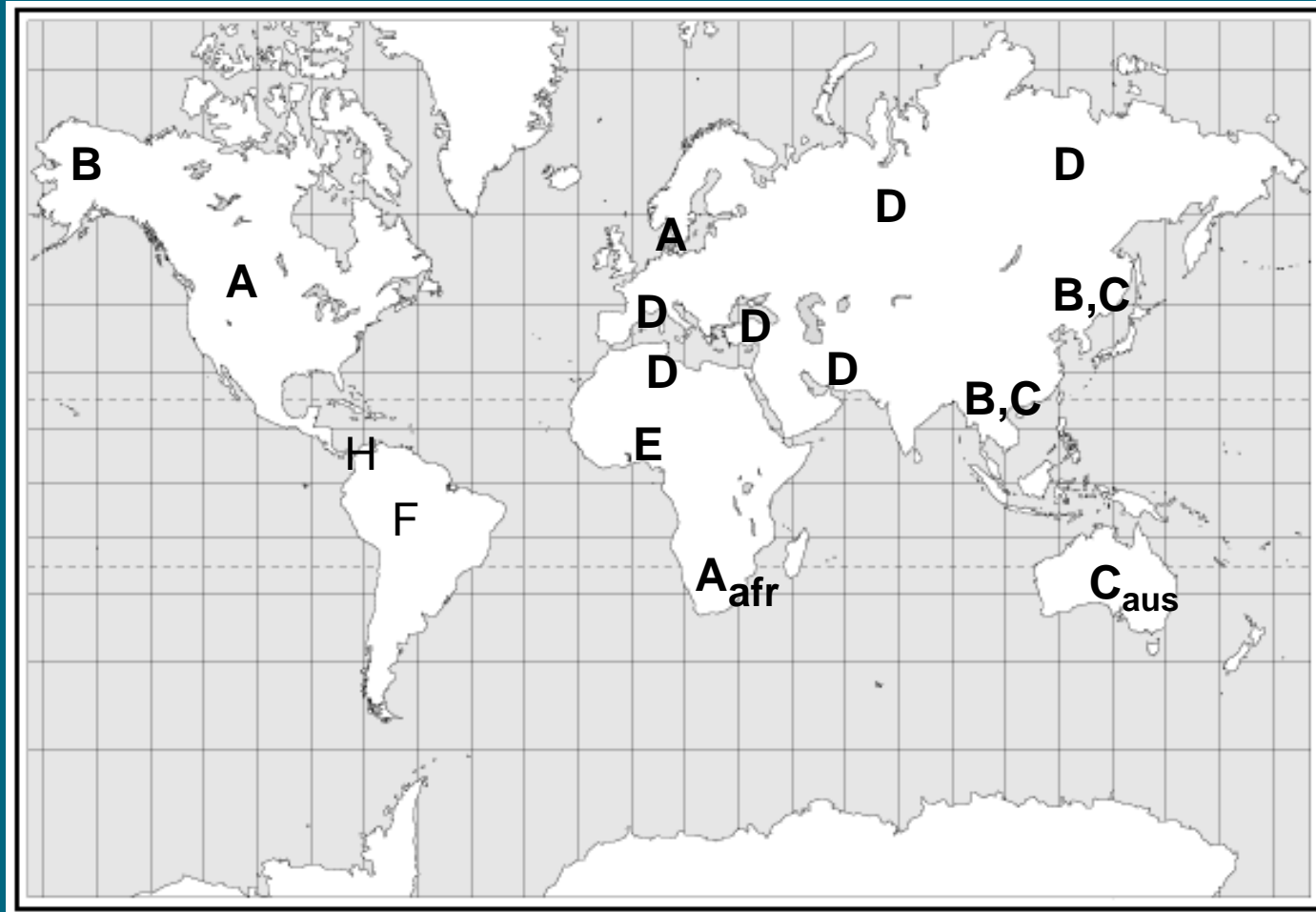
Why is HBV molecular typing important?

- Effectiveness of targeted vaccination programs
- Identification of new transmission routes
- Fast detection of central (medical) infection source
- Spread of antigenic variants
- Spread of antiviral resistance



Is the current Dutch HBV control policy effective?

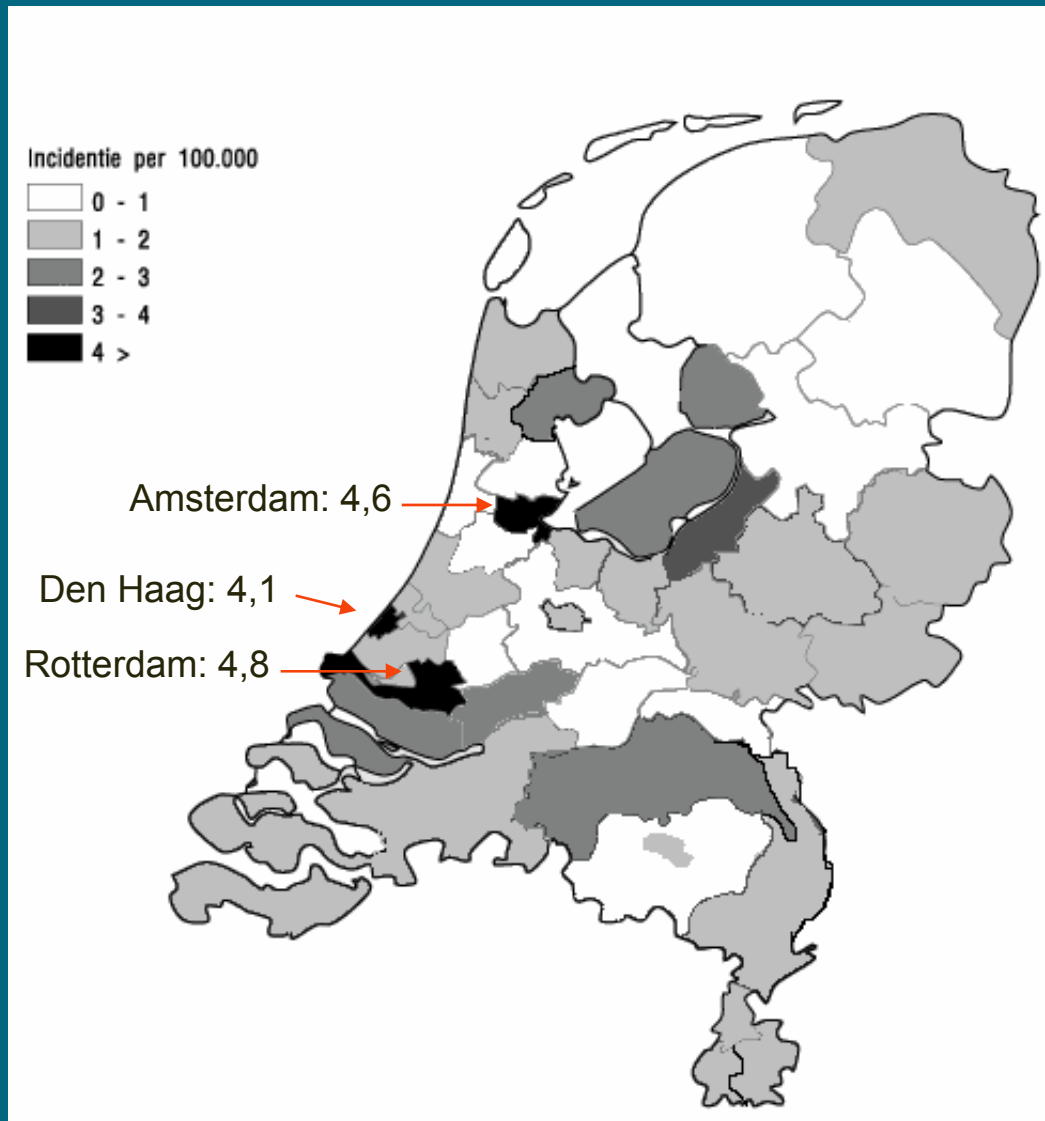
Geographic distribution of HBV genotypes



How different are the HBV genomes?

- 8 different genotypes are known (A – H, 8% nt difference)
- Variation is depending on the position on the genome
- Many subdivision within a genotype
 - gA1 [Africa] and gA2 [MSM]
 - gD of Intravenous Drugs Users differs from immigrants
 - Ba (recom.) and Bj in Japan
- Phenotypic and clinical differences between genotypes

Acute HBV incidence in the Netherlands



Average incidence: 1.8 / 100.000

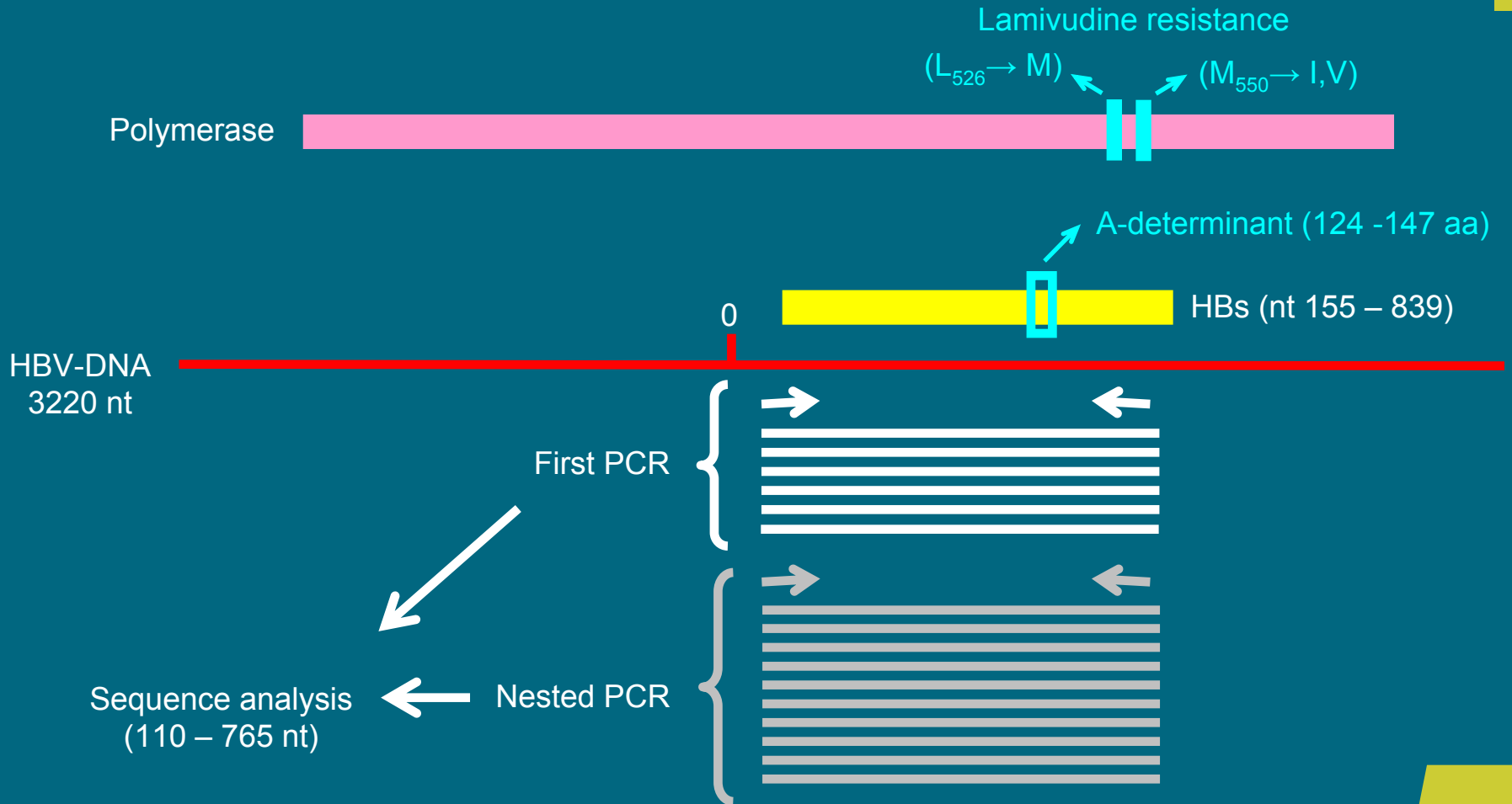
~300 cases/y → ~1000 inf./y

Male vs. Female: 5 vs. 1

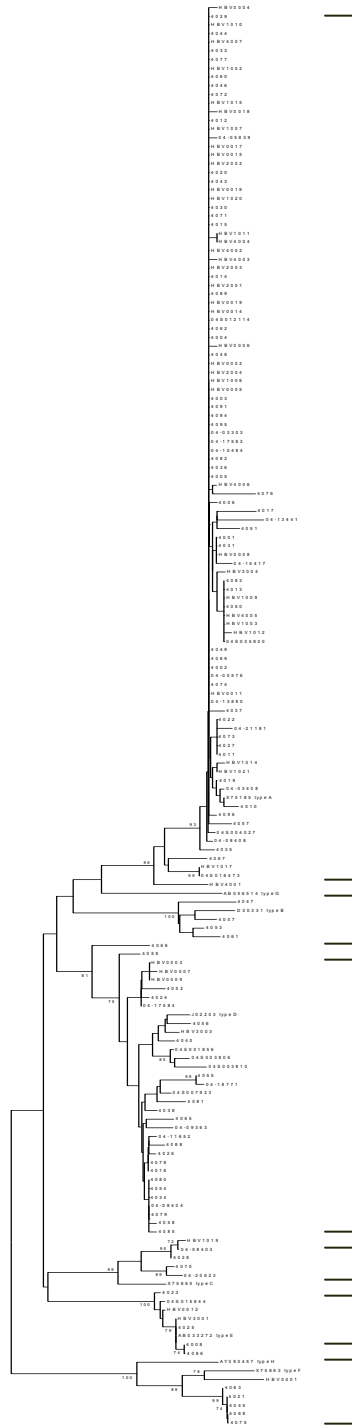
Most likely source of transmission of acute HBV

Source	Database (Osiris, n=1060)
Sexual	60%
MSM	34%
Heterosexual	23%
Other	3%
Vertical	1%
Accidents	2%
IDU	1%
Other	11%
Unknown	25%

Genomic organization of HBV



Acute HBV in The Netherlands (2004)



Genotype A

Europe, North America

Genotype B

South-east Asia

Genotype D

Mediterranean

Genotype C

Asia

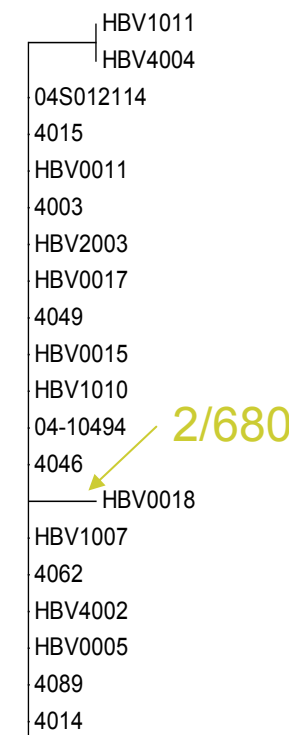
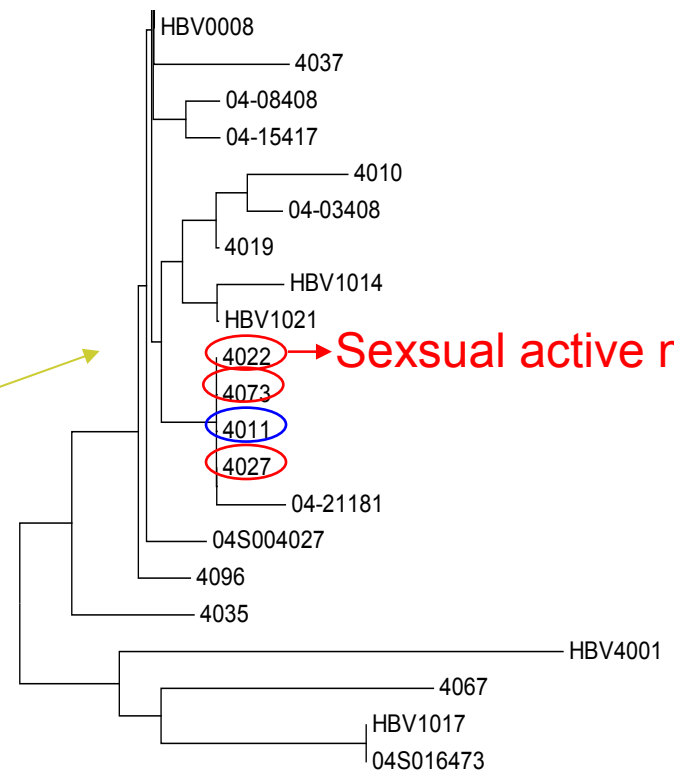
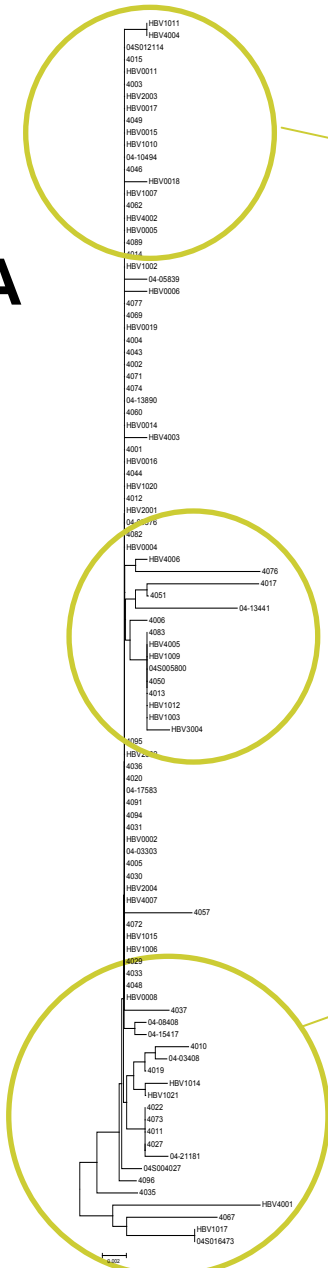
Genotype E

Africa

Genotype F

South America

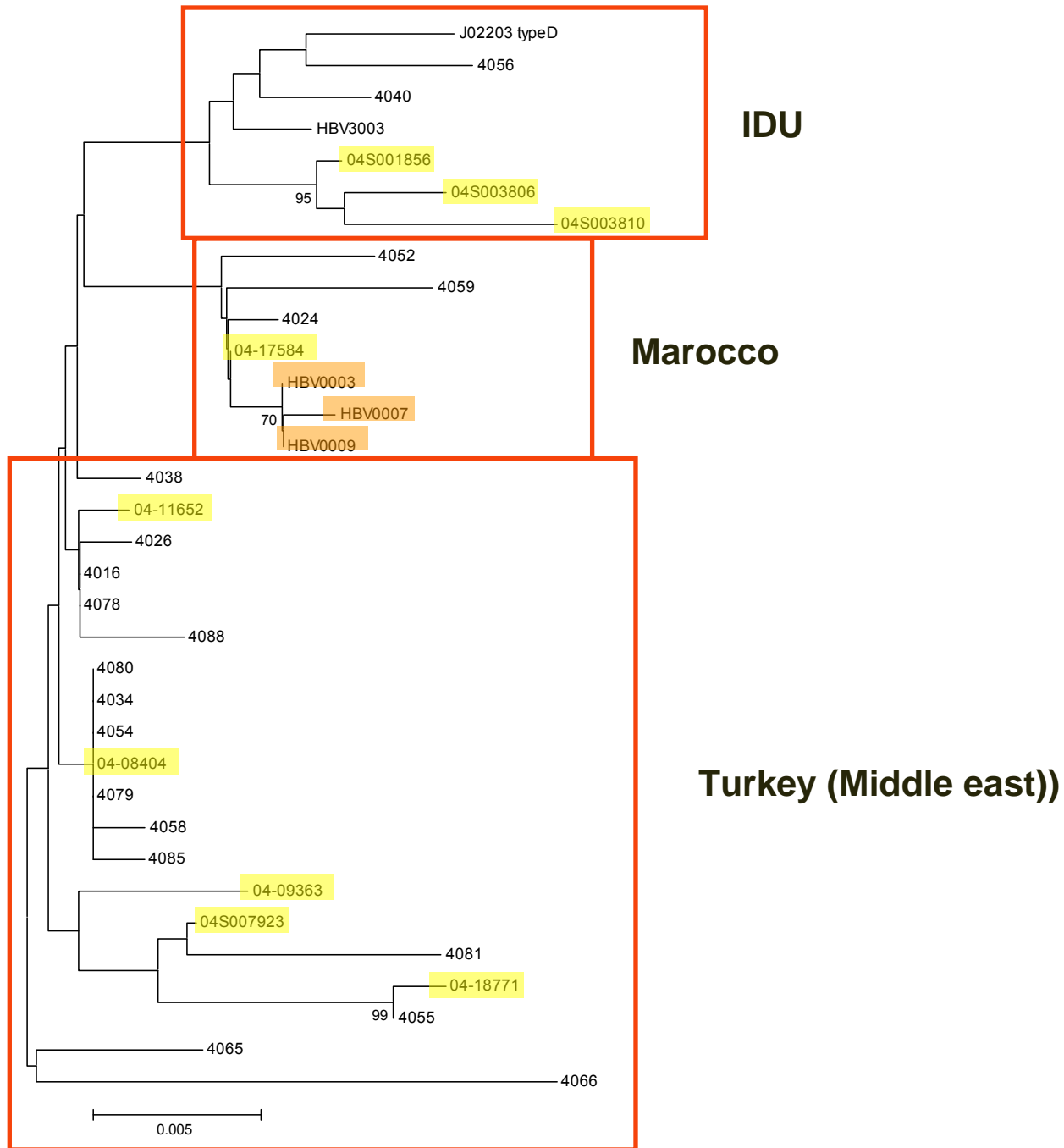
gA



Sexual active man from Dutch Caribbean

2/680

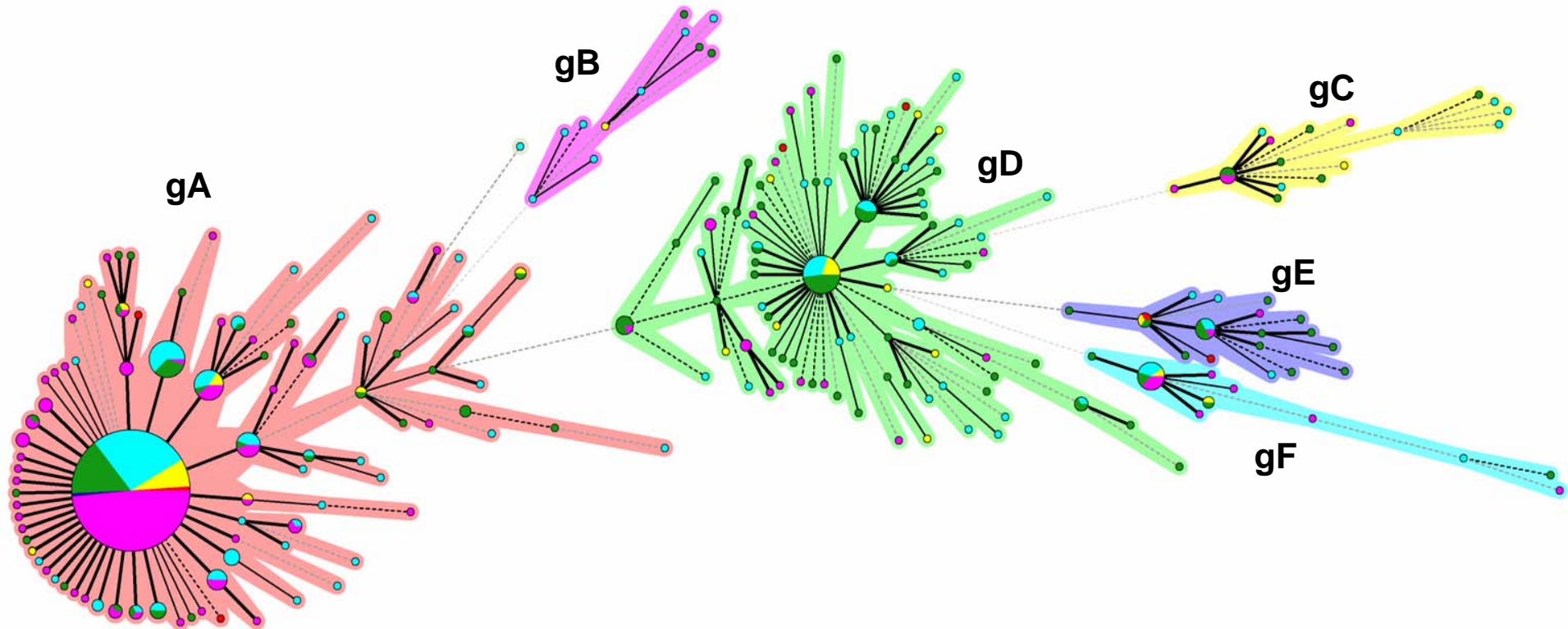
gD



Incidence of genotypes in acute HBV

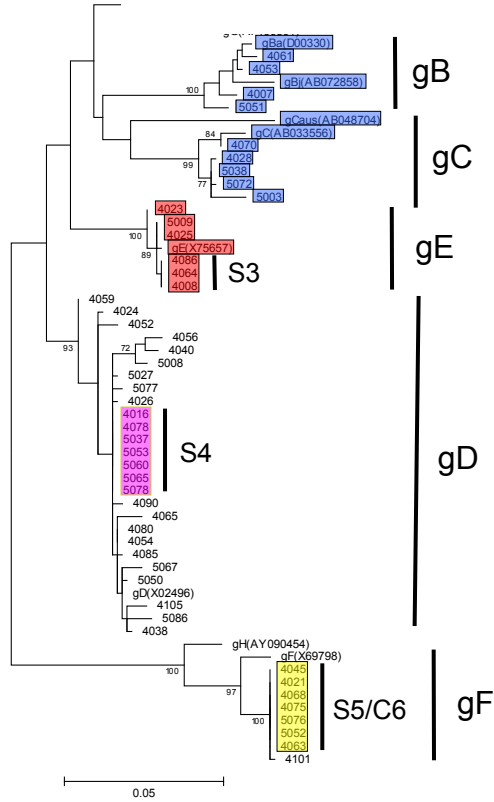
<i>Genotypes</i>	<i>Total (acute)</i>	<i>Male</i>	<i>Female</i>
gA	65%	309	55
gB	2%	6	5
gC	3%	19	-
gD	22%	77	48
gE	4%	13	11
gF	4%	15	6
gG (+ gA)	0%	2	-
gH	0%	-	-
<i>n=</i>	<i>579</i>	<i>441</i>	<i>125</i>

Minimal spanning tree of acute HBV isolates (2004-2007, n= 579)

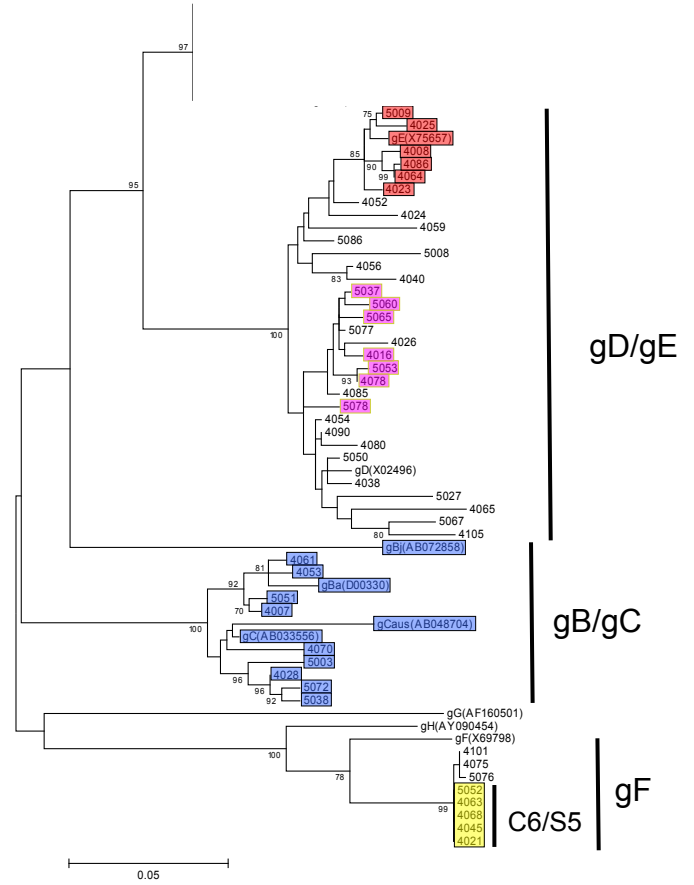


Pink	= MSM
Green	= Heterosexual
Yellow	= Other
Blue	= Unknown

S region

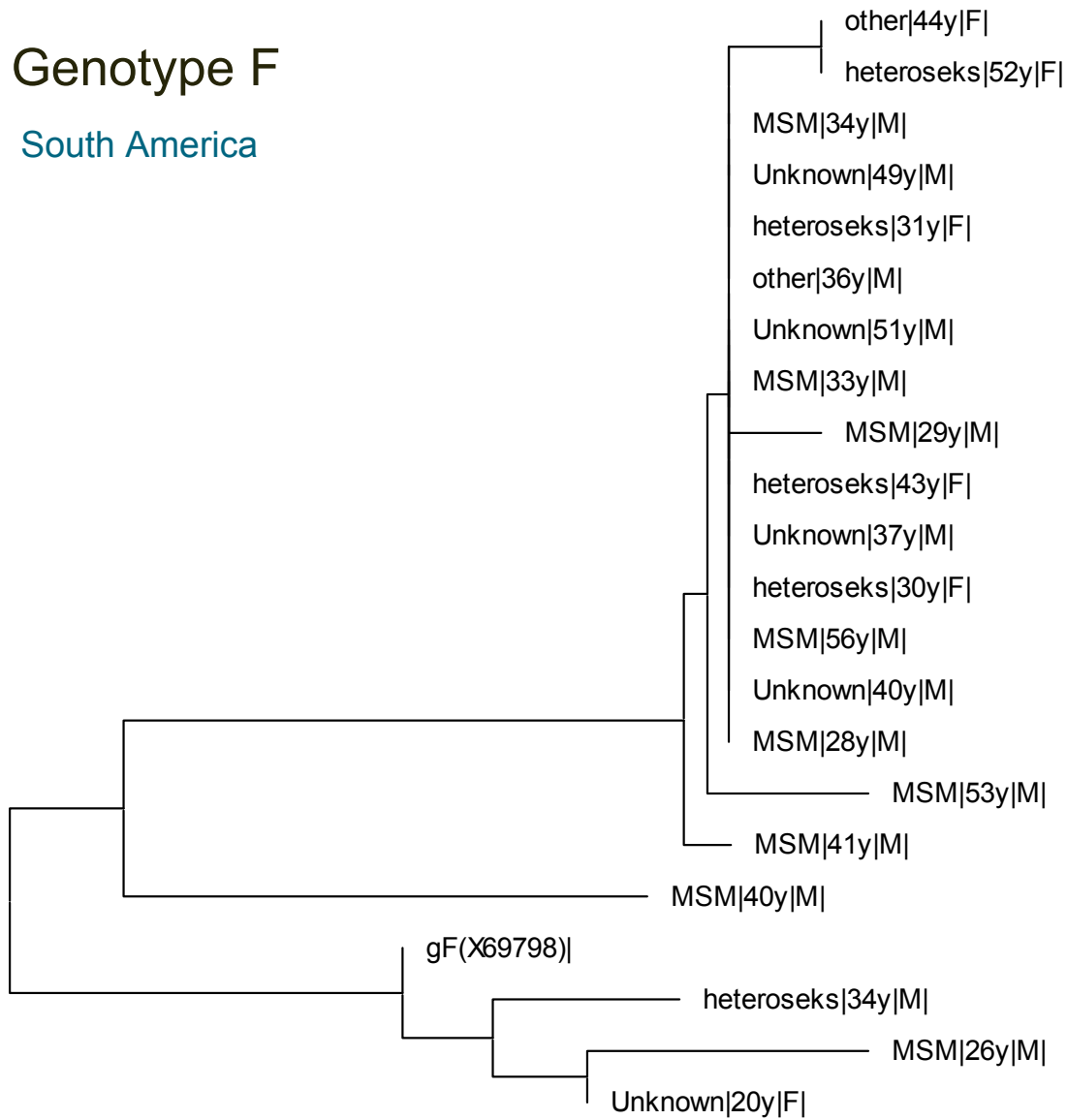


C region



Genotype F

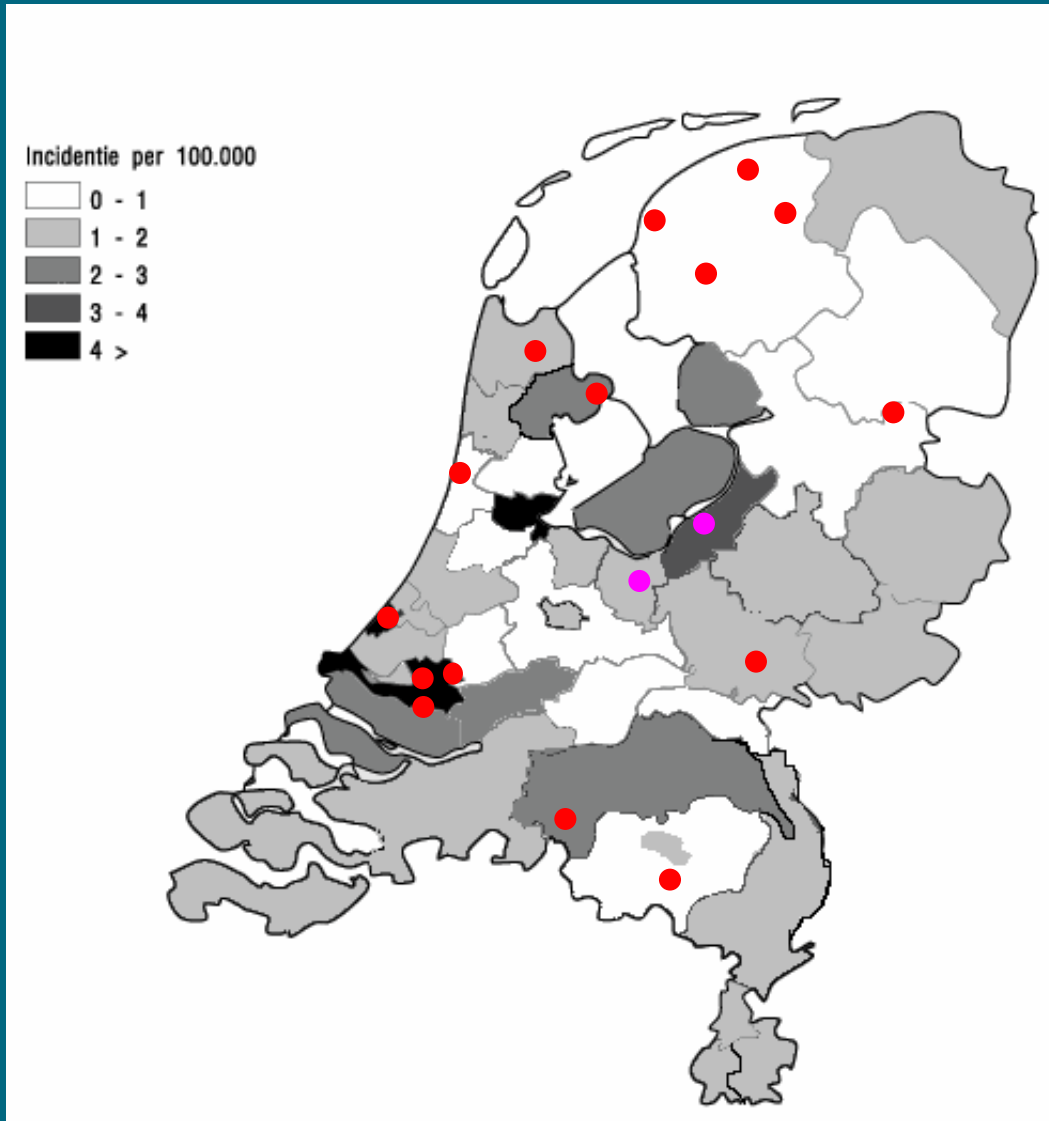
South America



0.002

RIVM

HBV genotype F cluster (2004 – 2008)



Netherlands: 21/579 (4%)

Friesland: 4/17 (24%)

HBV mutants

	HBV infection	
	Acute	Chronic
Reported cases (Jan. 2004 - July 2008)	~1160	~6800
S-region sequence	583	312
Immune escape mutation (G145R)	0	0
Antiviral resistance (M550V)	2	2

HBV molecular typing of HBV

- Effectiveness of targeted vaccination programs:
Reduction in number of MSM gA-isolates (non sig.)
- Identification of new infection sources:
No new extensive transmissions have been found
- Spread of antigenic variants:
Only associated with use of HB-immunoglobuline
- Spread of antiviral resistance:
Low frequency among acute and chronic HBV



- Femke Koedijk
- Eline Op de Coul
- Jeroen Cremer
- Marita van de Laar
- Susan Hahné



- Robin van Houdt
- Sylvia Bruisten
- Nicole Dukers
- Anneke van den Hoek
- Roel Coutinho



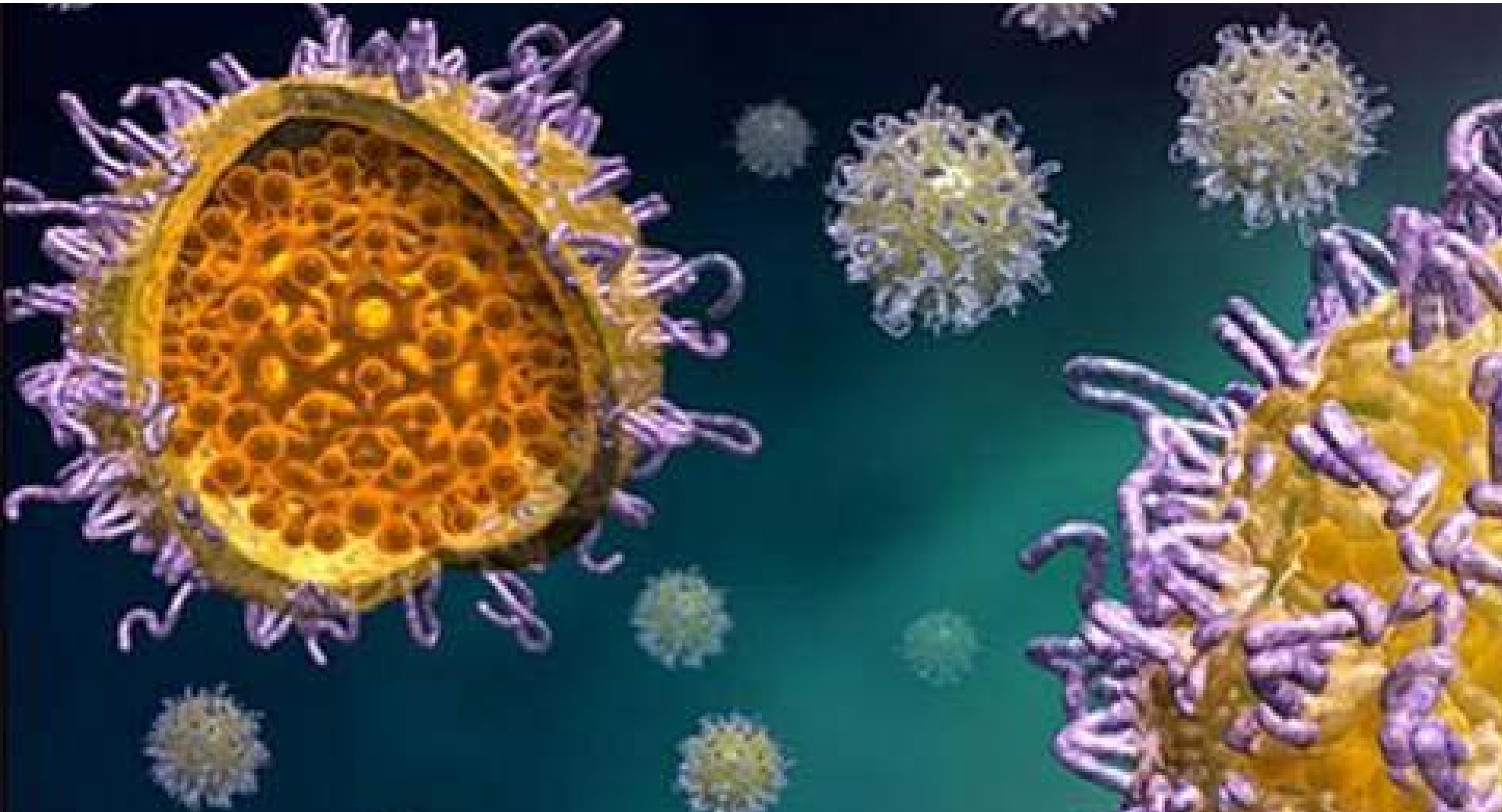
- Irene Veldhuizen
- Marijke Mosterd
- Hannelore Götz
- Jan Hendrik Richardus



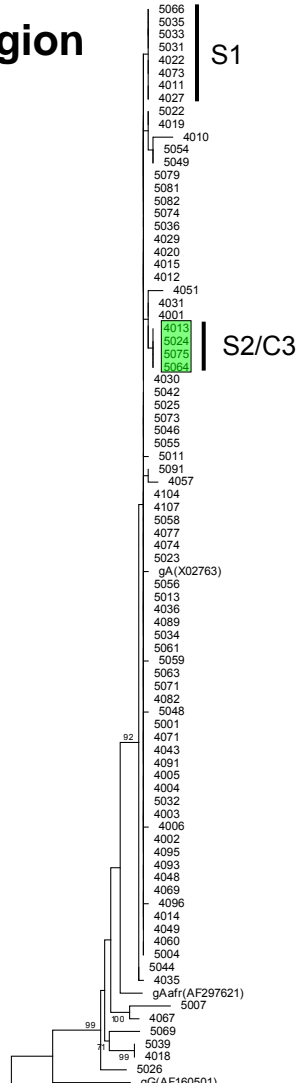
- Martin Schutten
- Bert Niesters
- Rob de Man
- Gerard van Doornum

Molecular epidemiology of HBV in The Netherlands

Hein J. Boot

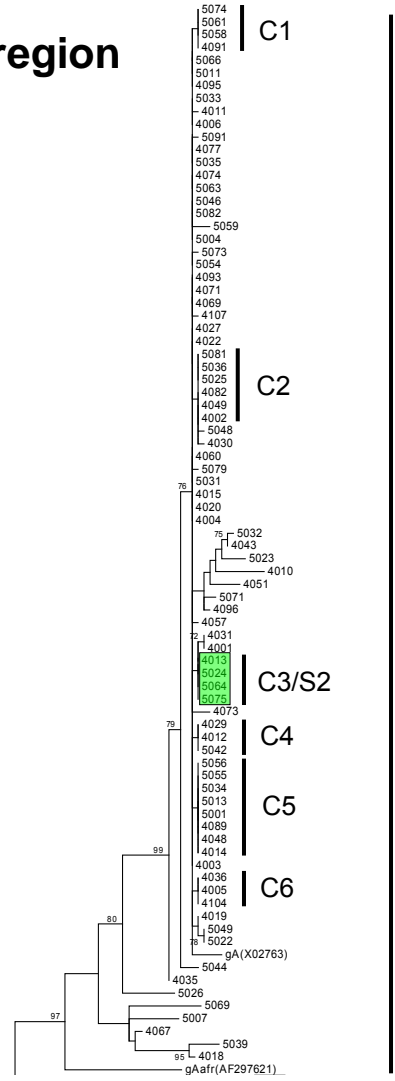


S region



gA

C region



gA