

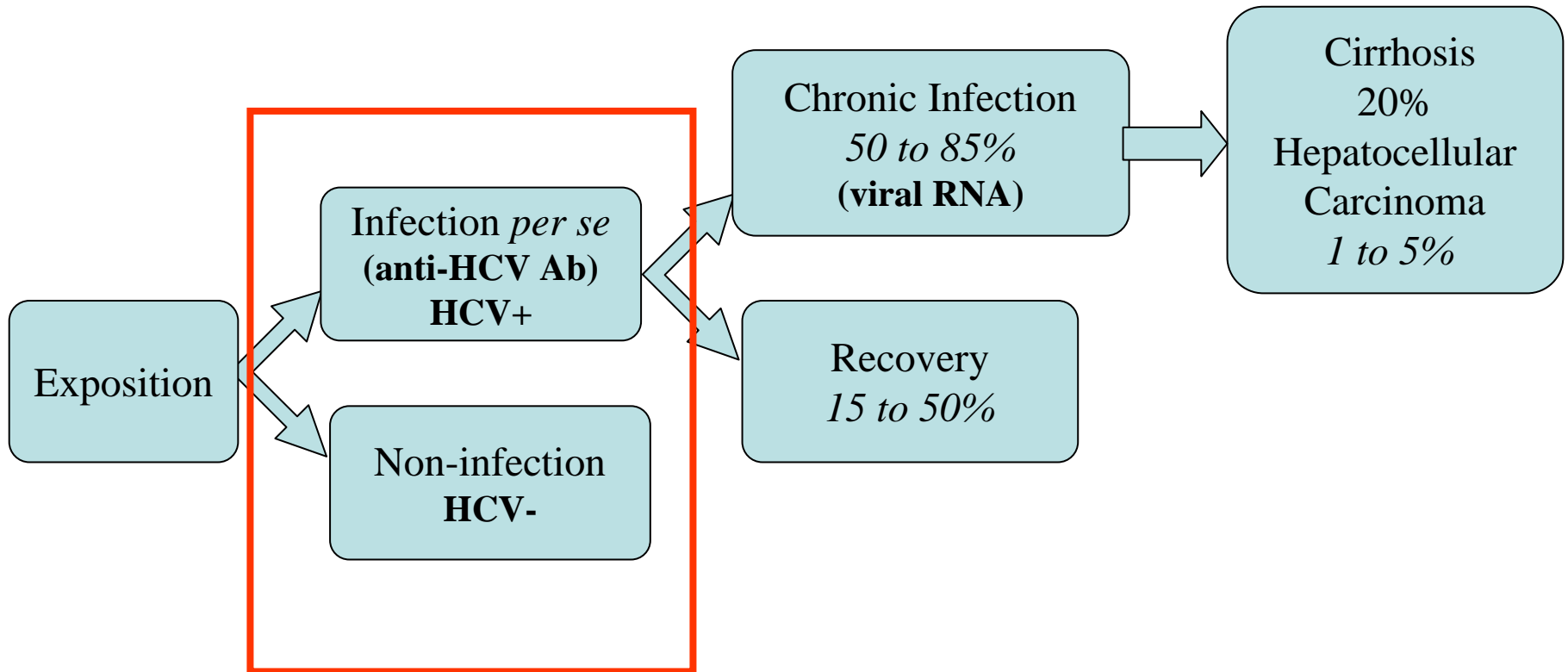
**Linkage analysis for Hepatitis C virus
infection in an endemic population
from rural area
(ANRS 1270)**

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Natural history of HCV infection



Familial study in Egypt

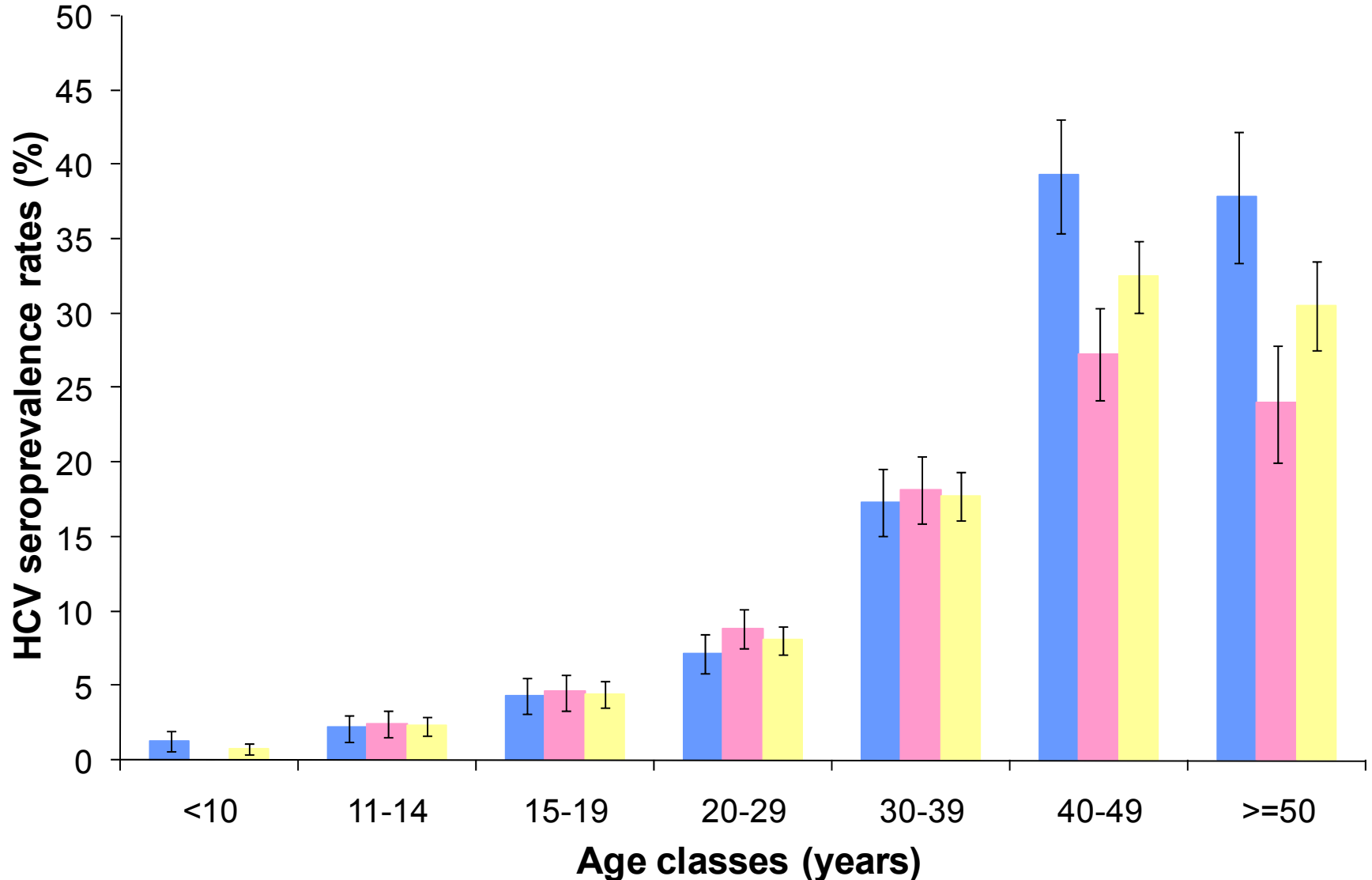


- **Zawiat Razin, Egypte**
 - Nile Delta
 - ~ 5500 individus
- **Collected data (2003 – 2005)**
 - **Epidemiology :**
 - potential risk factors (age, sex, medical and surgical history, blood transfusion ...)
 - **Biology**
 - **Serology : phenotype HCV+/HCV-**
 - **Genetic : familial links (pedigrees)**

Familial data

- **816 households**
- **1631 nuclear families (=5516 inhabitants)**
- **3703 subjects (1796 women, 1907 men)**
- **aged from 3 to 88 years old**
- **clustered in 312 families from 3 to 270 members**
- **overall HCV seroprevalence = 12.3%**

HCV seroprevalence according to age and gender



Previous results

- **Known associated risk factors**

- Age
- Parenteral anti-schistosomiasis trt
- Blood transfusion
- Instrumental delivery
- Gum treatment

($p < 10^{-4}$)

($p < 10^{-4}$)

($p < 10^{-4}$)

($p = 0.01$)

($p = 0.03$)

≥ 20 yo only

Arafa et al. J Hepatol 2005

Previous results

- **Known associated risk factors**

- Age (p<10⁻⁴)
 - Parenteral anti-schistosomiasis trt (p<10⁻⁴)
 - Blood transfusion (p<10⁻⁴)
 - Instrumental delivery (p=0.01)
 - Gum treatment (p=0.03)
- } **≥ 20yo only**

Arafa et al. J Hepatol 2005

- **Familial dependences**

Dependences	Number of clusters	OR [95%CI]	p
Father-Mother (FM)	325	2.2 [1.3-3.6]	<2.10 ⁻³
Father-Offspring (FO)	297	3.4 [1.8-6.2]	<10 ⁻⁴
Mother-Offspring (MO)	401	3.8 [2.5-5.8]	<10 ⁻⁸
Sib-Sib (SS)	383	9.3 [4.9-17.6]	<10 ⁻¹⁰

Plancoulaine et al. Gut 2008

Segregation analysis

Observed familial distribution
of the phenotype (HCV+/HCV-)



Expected familial distribution
of the phenotype (HCV+/HCV-)

Under different hypotheses
of familial transmission

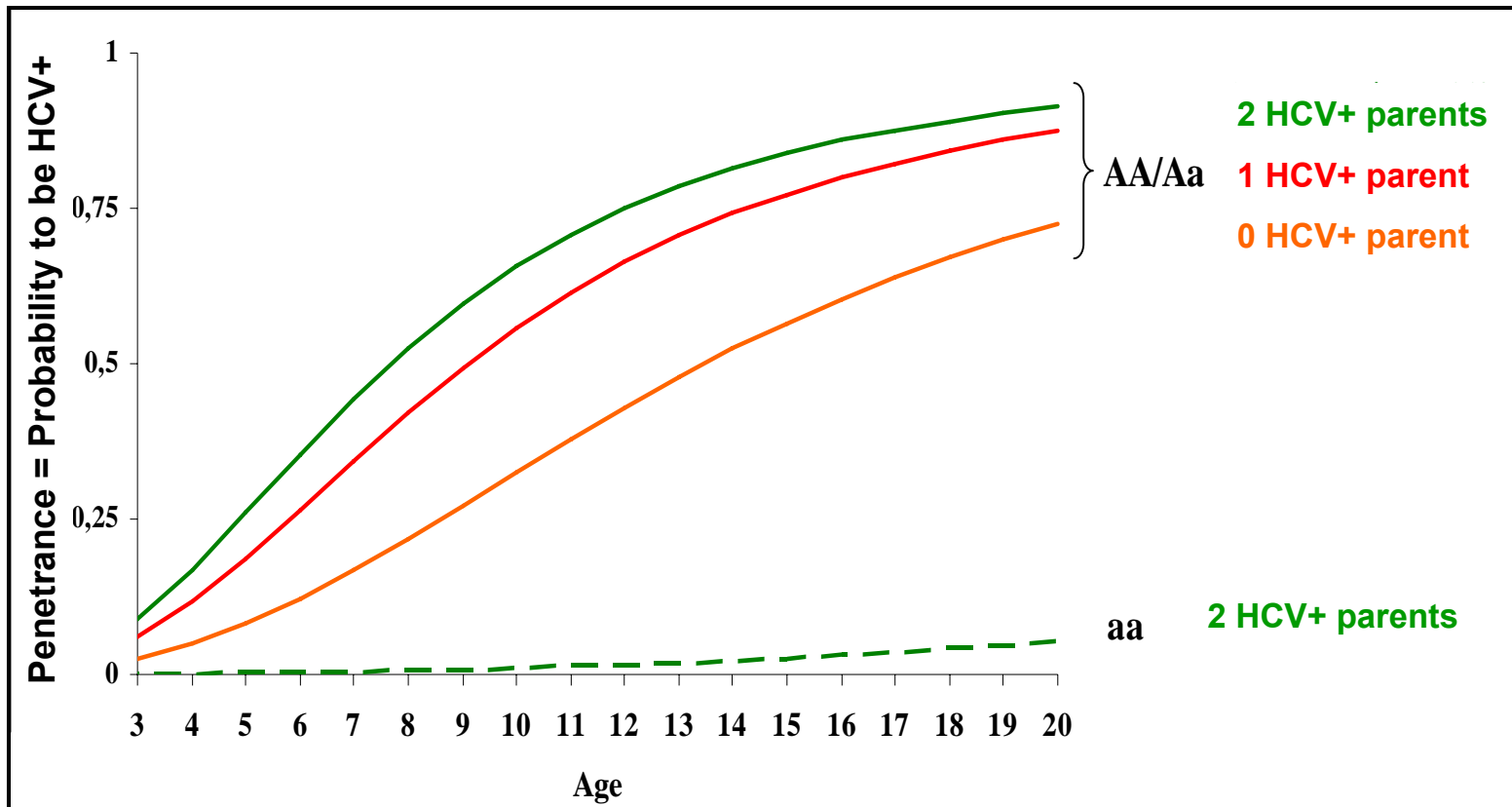
Allows to take **simultaneously** into account

- Known risk factors
- Familial correlations
- Diallelic (A, a) major gene effect : q, penetrances

Dominant gene explaining HCV infection in young (<20 yo)

Frequency of the predisposing allele A, $q = 0.013$

⇒ ~2.6% of the population is predisposed to HCV infection



Genome-wide linkage analysis

- **Data**

- families

- 48 families (252 to 206 ind), 533 individuals,
 - Available DNA for 411
 - Quality controls and sufficient call rate for 316 subjects = 173 males and 143 females

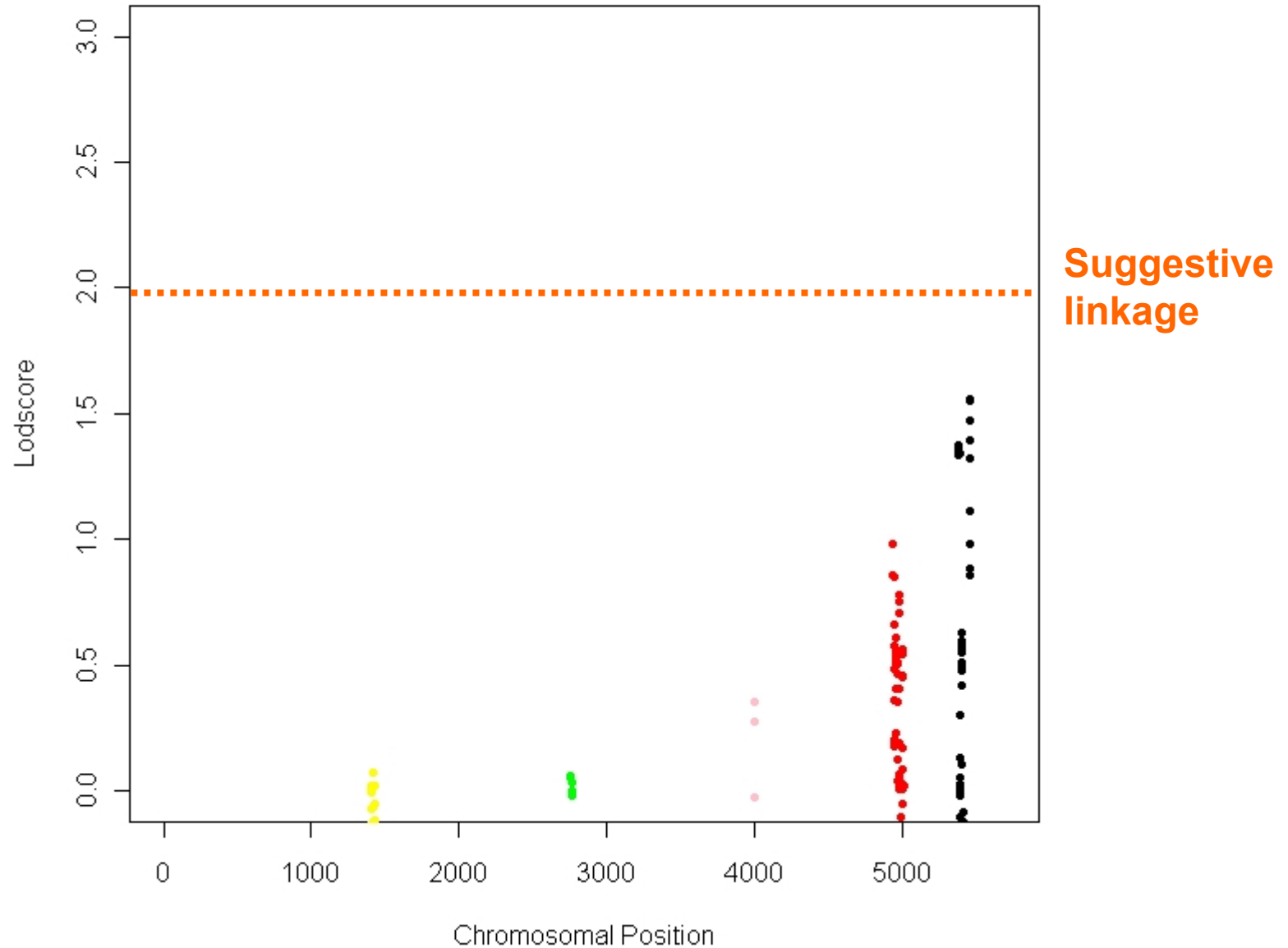
- 6047 SNPs (Illumina linkage IVb - CNG)

- 21 were excluded due to HWE $p < 0.001$, $MAF < 1\%$
 - 6021 analysed

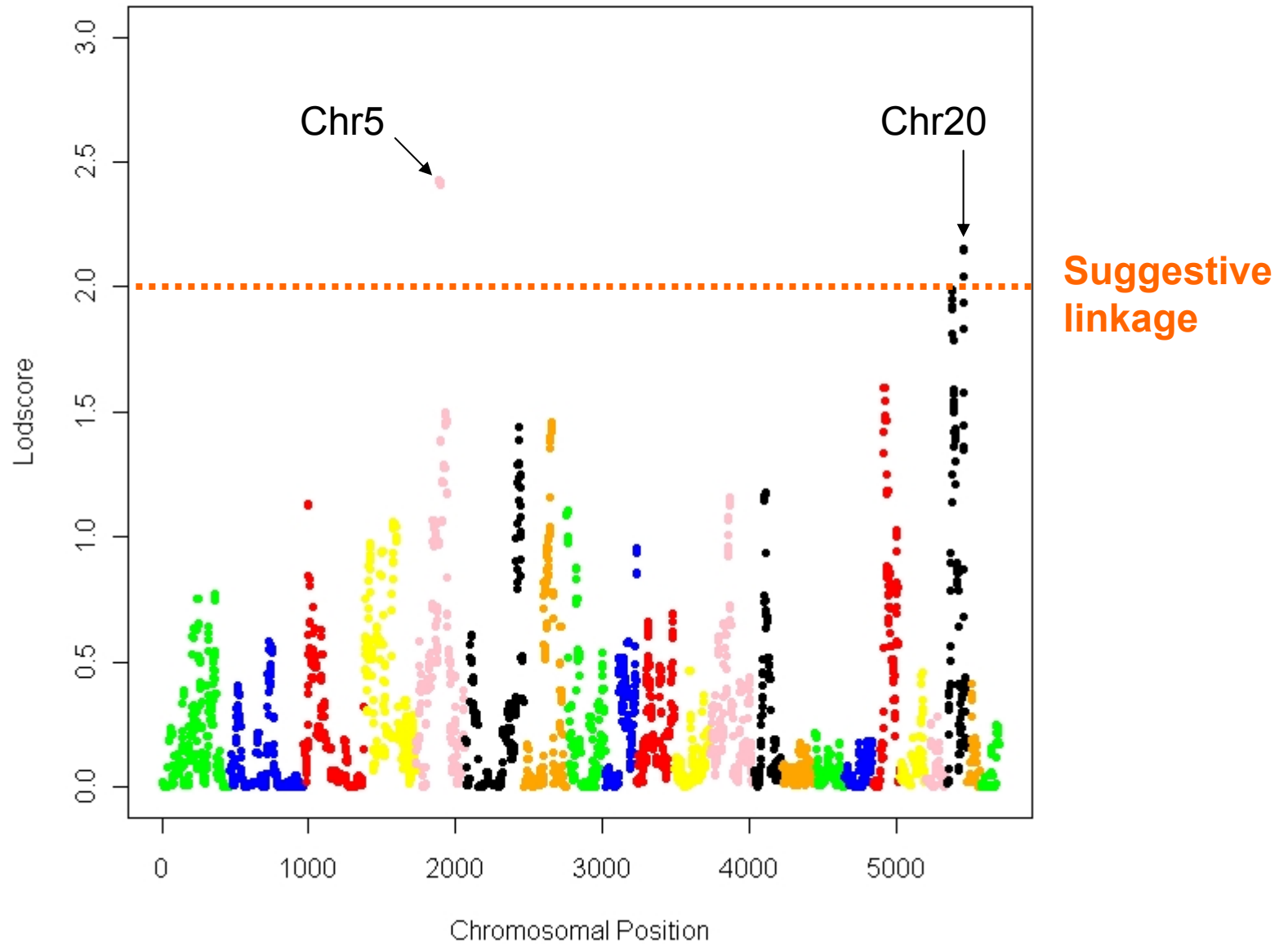
- **Linkage analysis**

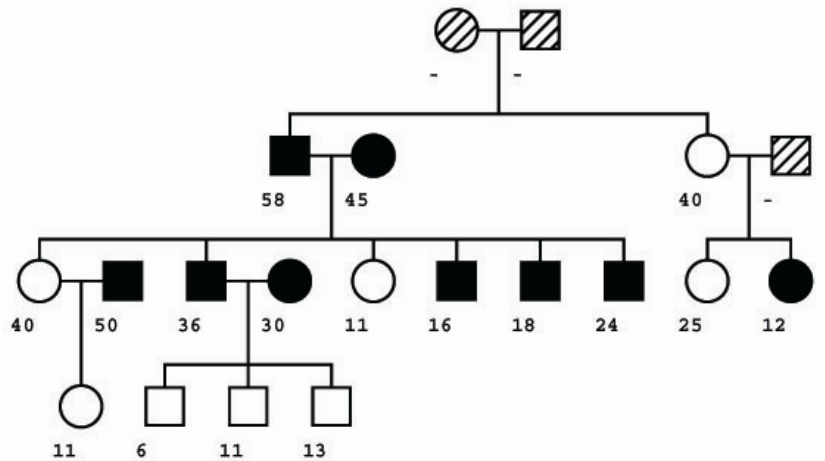
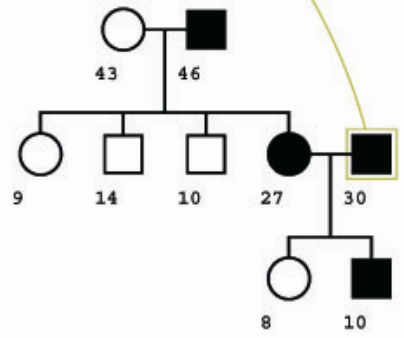
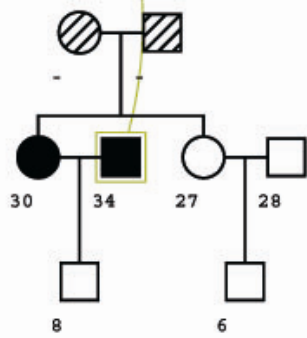
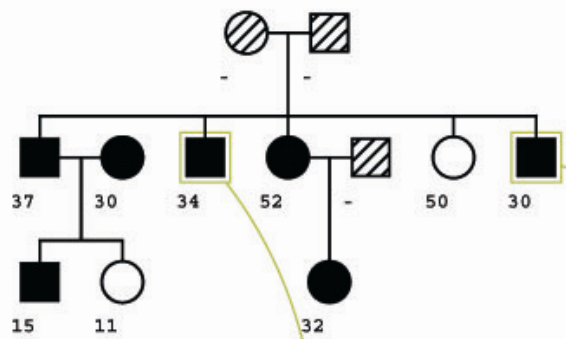
- Based on the model described previously (dominant, $q = 0.0013$)
 - Multipoints, taking into account age effect

Global analysis in 48 included families



Heterogeneity in families





age

 HCV-serology

 negative

 positive

 unknown

Perspectives

- Association study on infection status
 - Egyptian population
 - HCV infected (cleared or not) vs HCV uninfected (i.e. blood donors)
- Association study on clearance
 - To evaluate the role of those genes on clearance
 - Egyptian population
 - HCV chronically infected vs HCV cleared

Collaborators

- **Egypt**

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