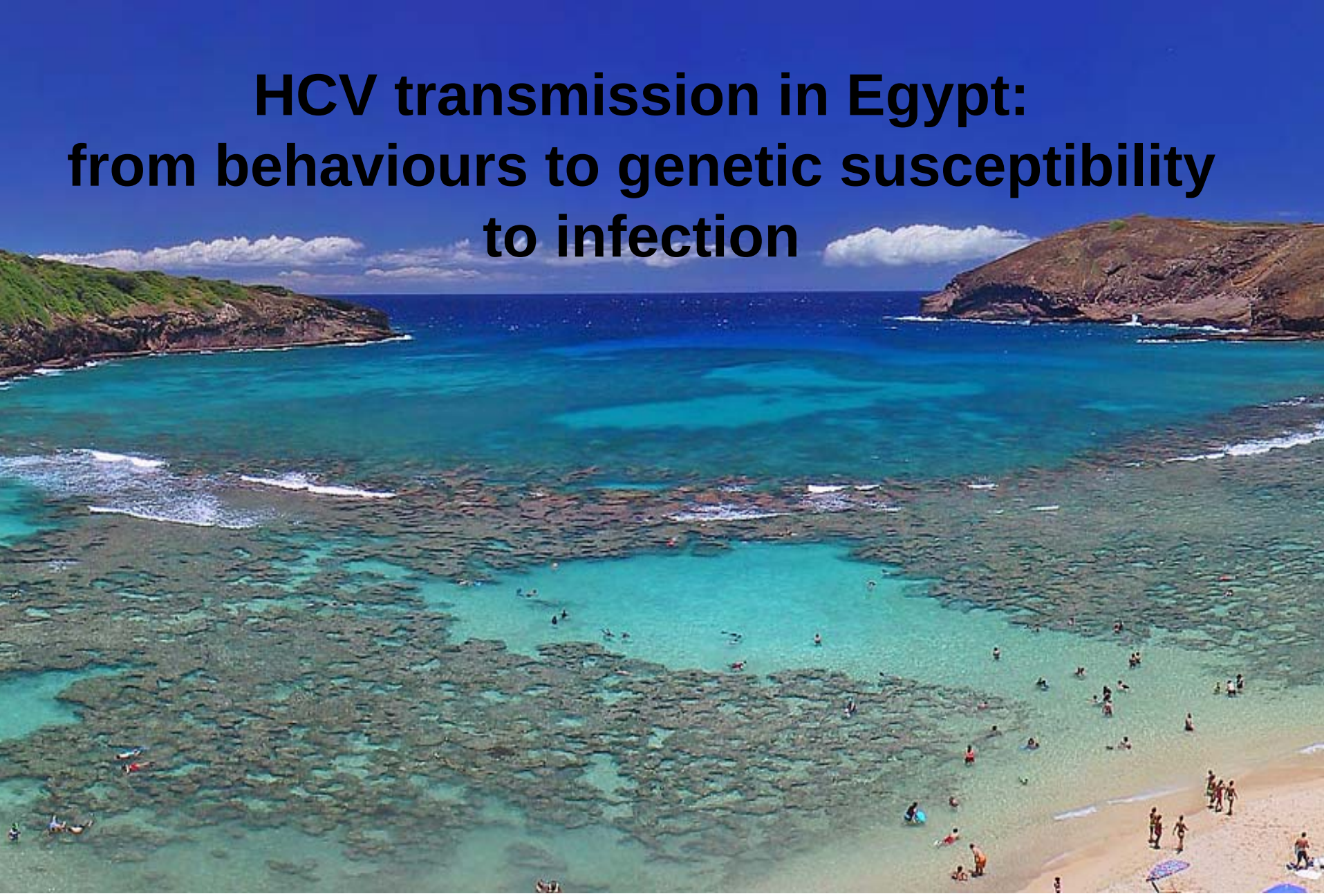
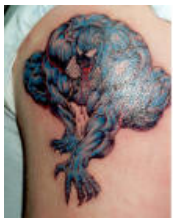
HCV transmission in Egypt: from behaviours to genetic susceptibility to infection



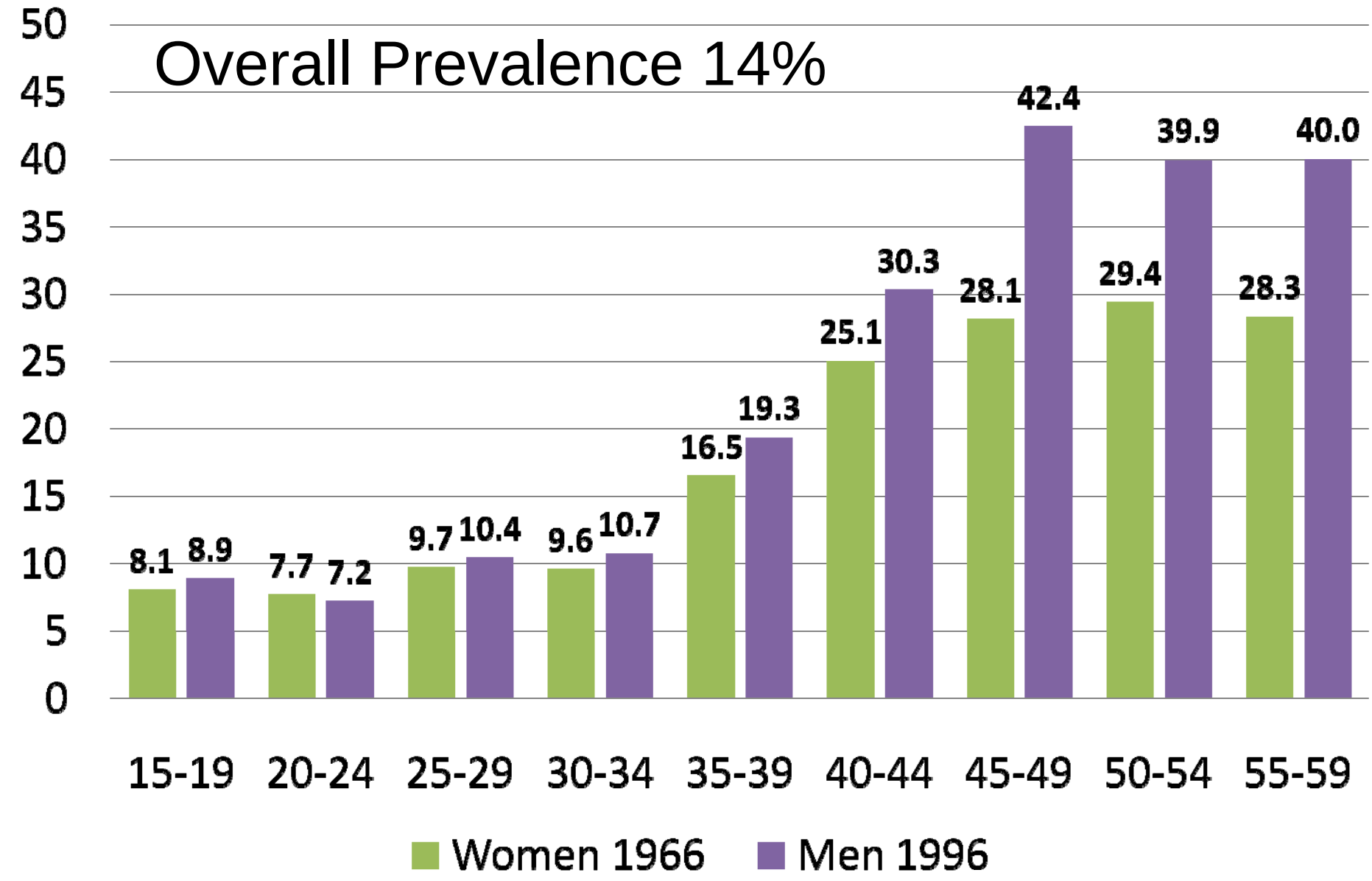
ANRS meeting - 23/01/2010

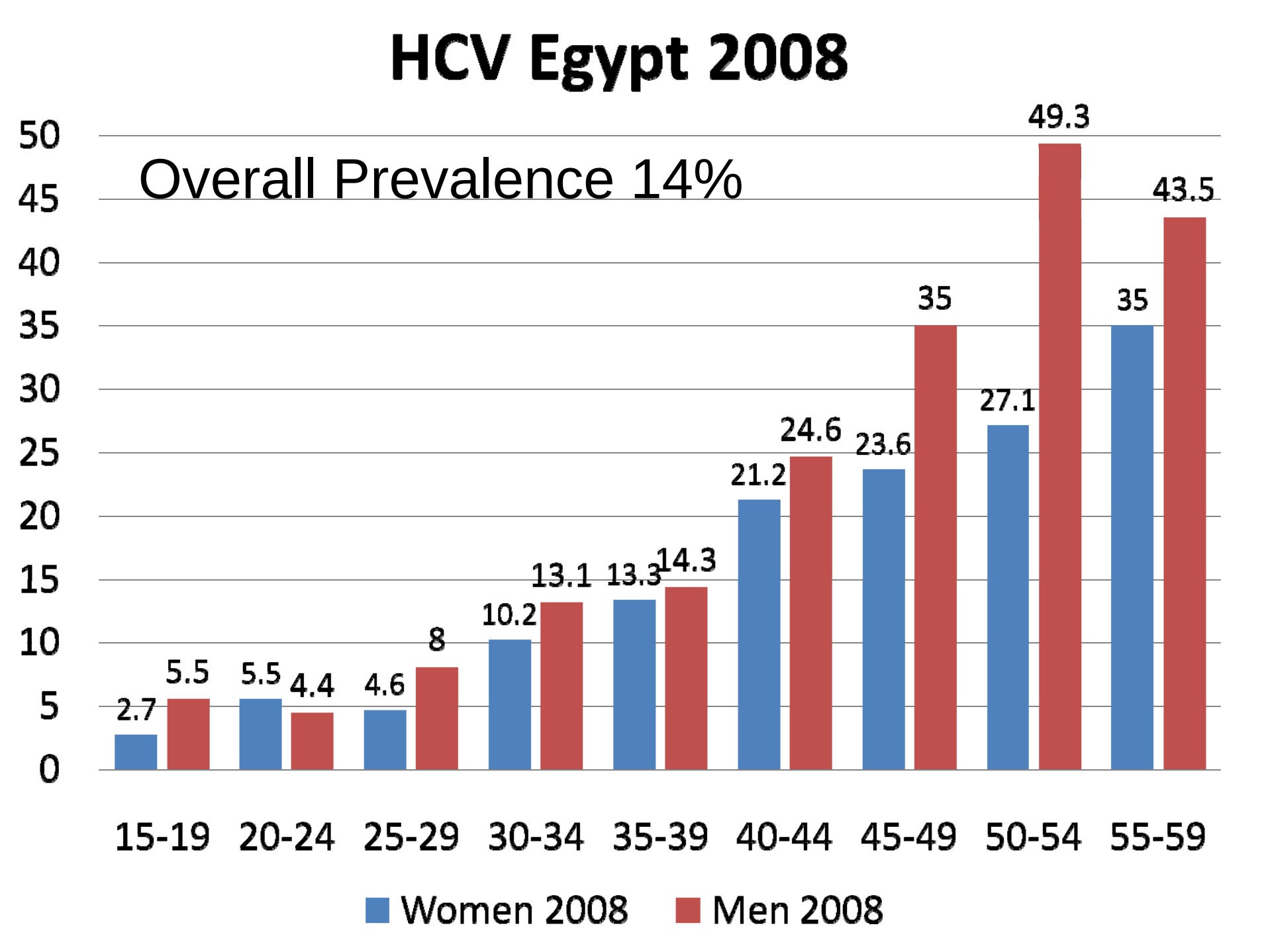
HCV transmission: Contact with infected blood



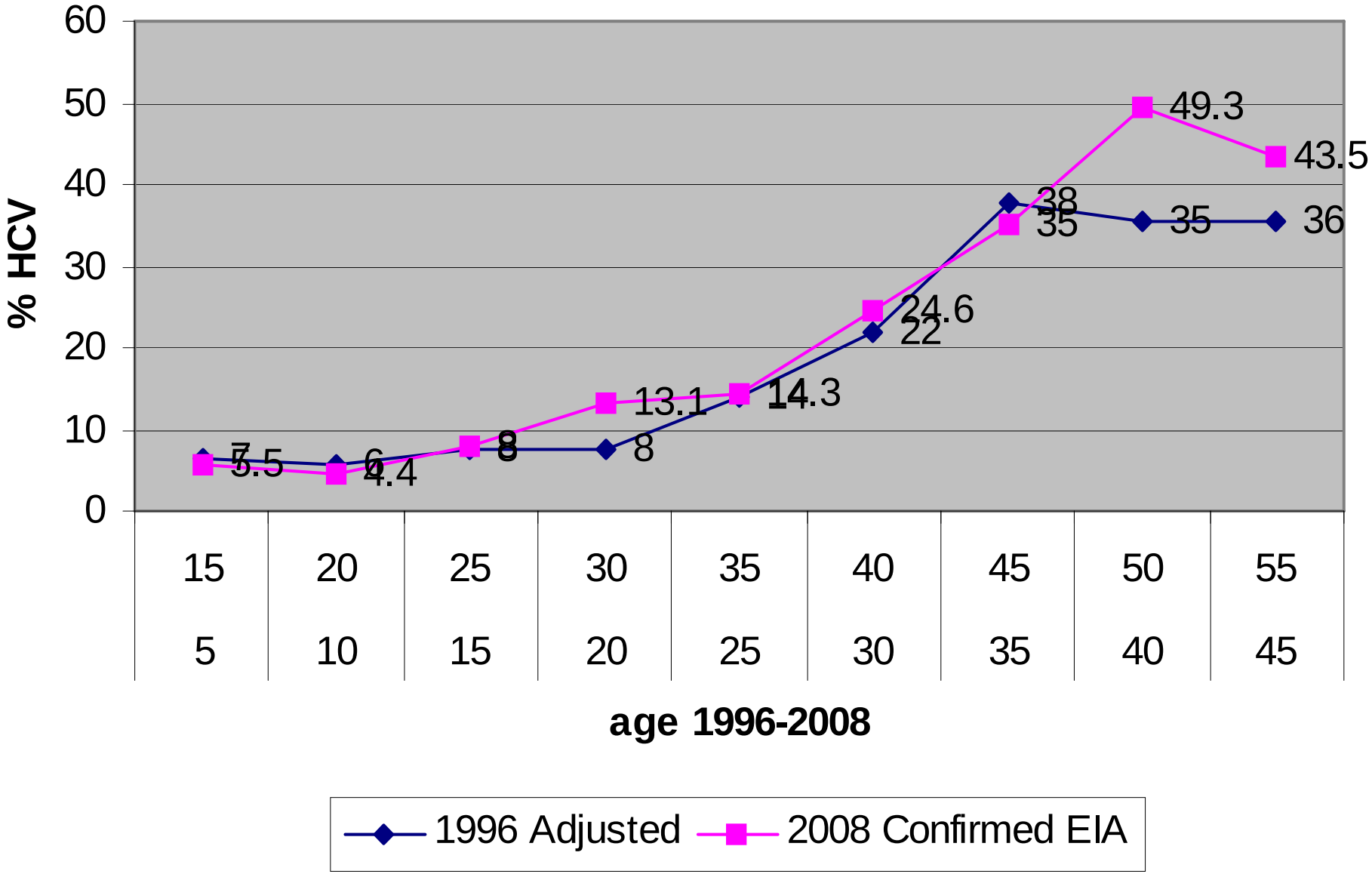
- **Blood transfusion**
- **Injections**: medical, illicit drug use
- **Invasive medical procedures**: surgery, endoscopy, …
- Tattoing, acupuncture, body-piercing, shaving,…
- Mother-to-infant
- Sexual

HCV Egypt 1996

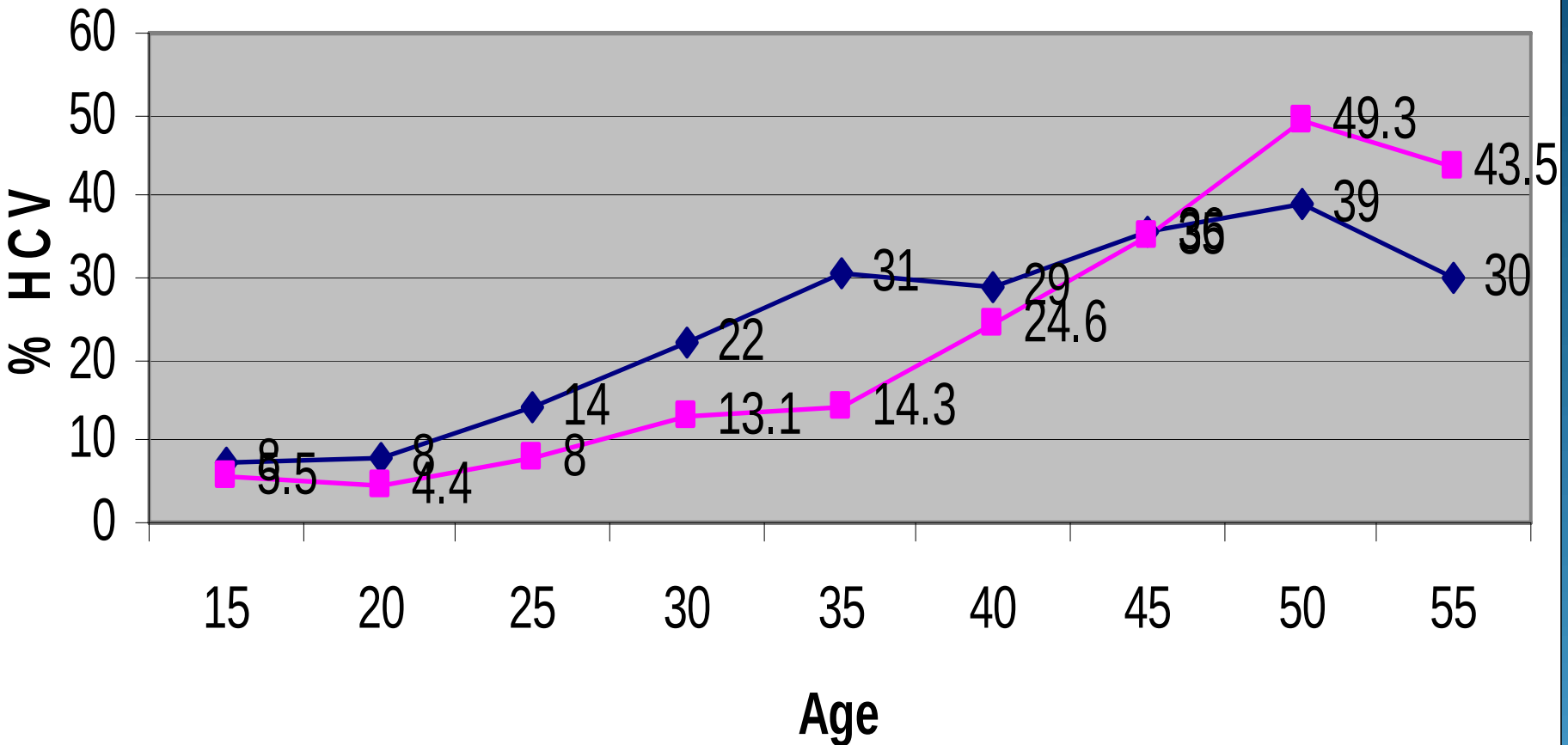



HCV Egypt 2008
Overall Prevalence 14%
50
45
40
35
30
25
20
15
10
5
0
2.7
5.5
5.5
4.4
4.6
8
10.2
13.1
13.3
14.3
21.2
24.6
23.6
35
27.1
49.3
35
43.5
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
Women 2008
Men 2008

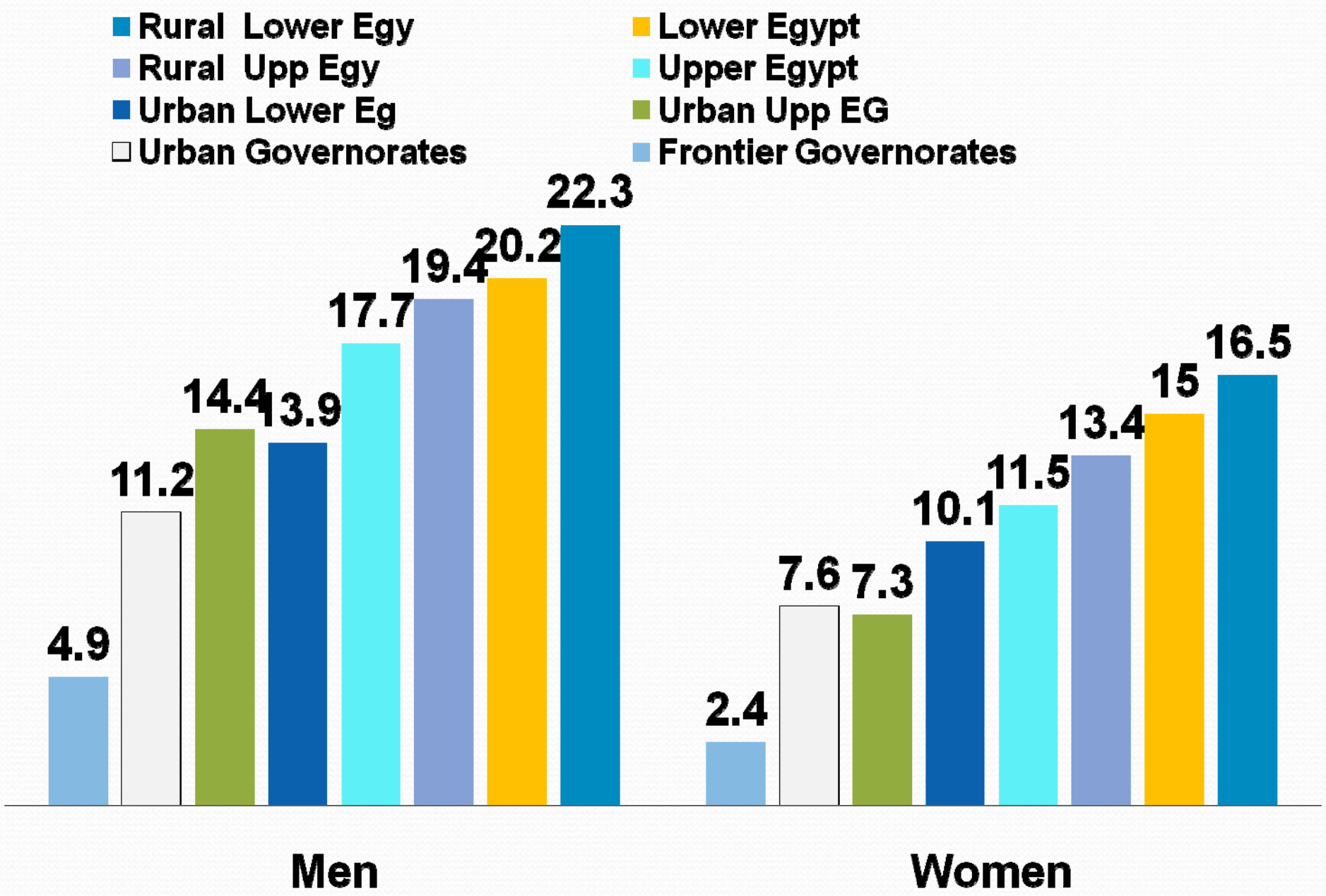
HCV Cohort prevalence 1996-2008



Comparison of HCV 1996-2008



HCV Egypt 2008



Questions

- What are the on-going modes of HCV transmission in Egypt?
- What is the contribution of intra-familial transmission?
- What about genetic susceptibility to infection?

On-going modes of HCV transmission
&
intra-familial transmission

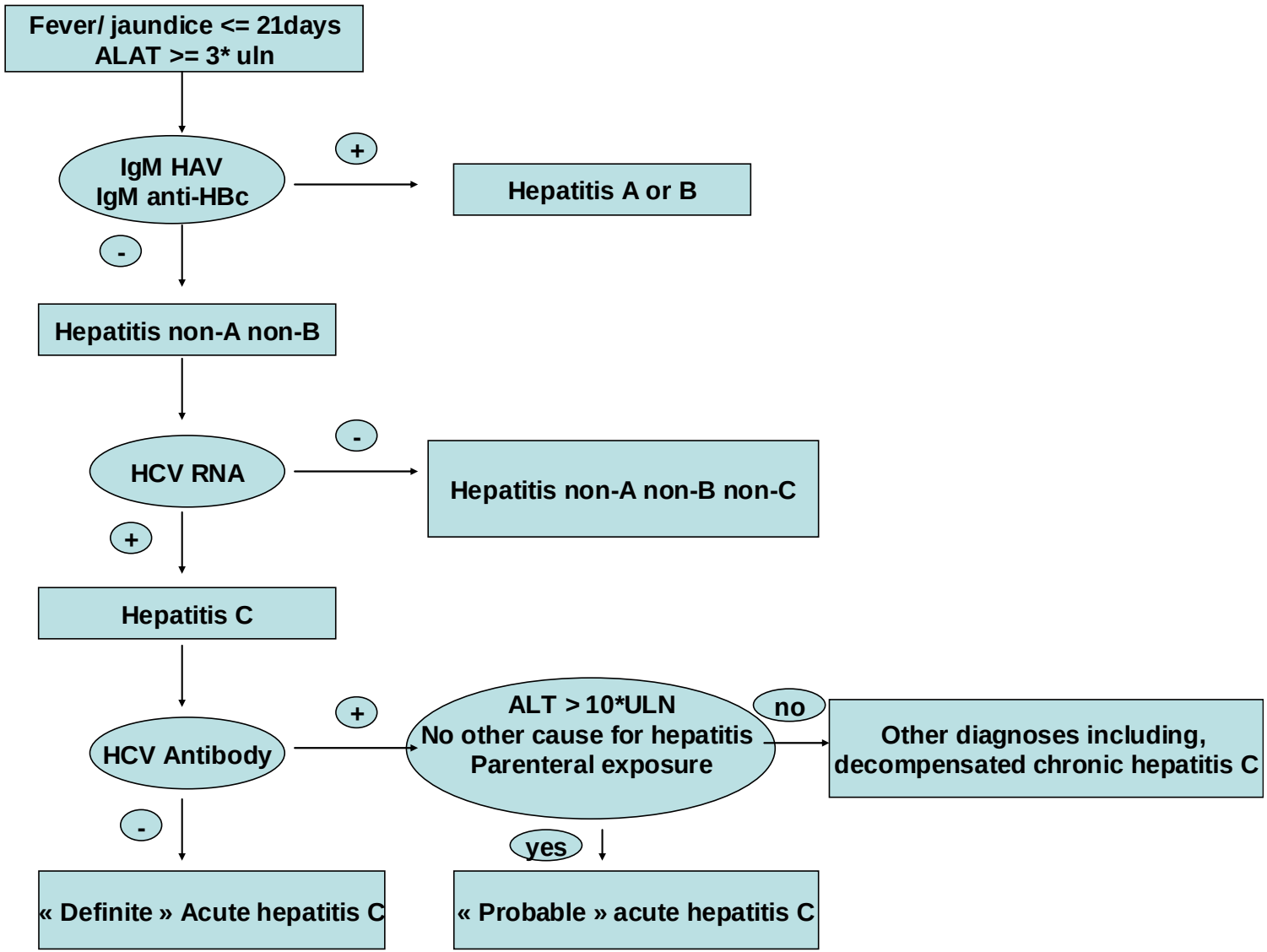
“Fever Hospitals” study (ANRS 12122)

- Importance of studying acute hepatitis C cases and not prevalent infections:
  - Well-defined « at risk » period for studying exposures (one to three months before onset of symptoms): data quality.
  - Tells you about « on-going » transmission, not that of the past years

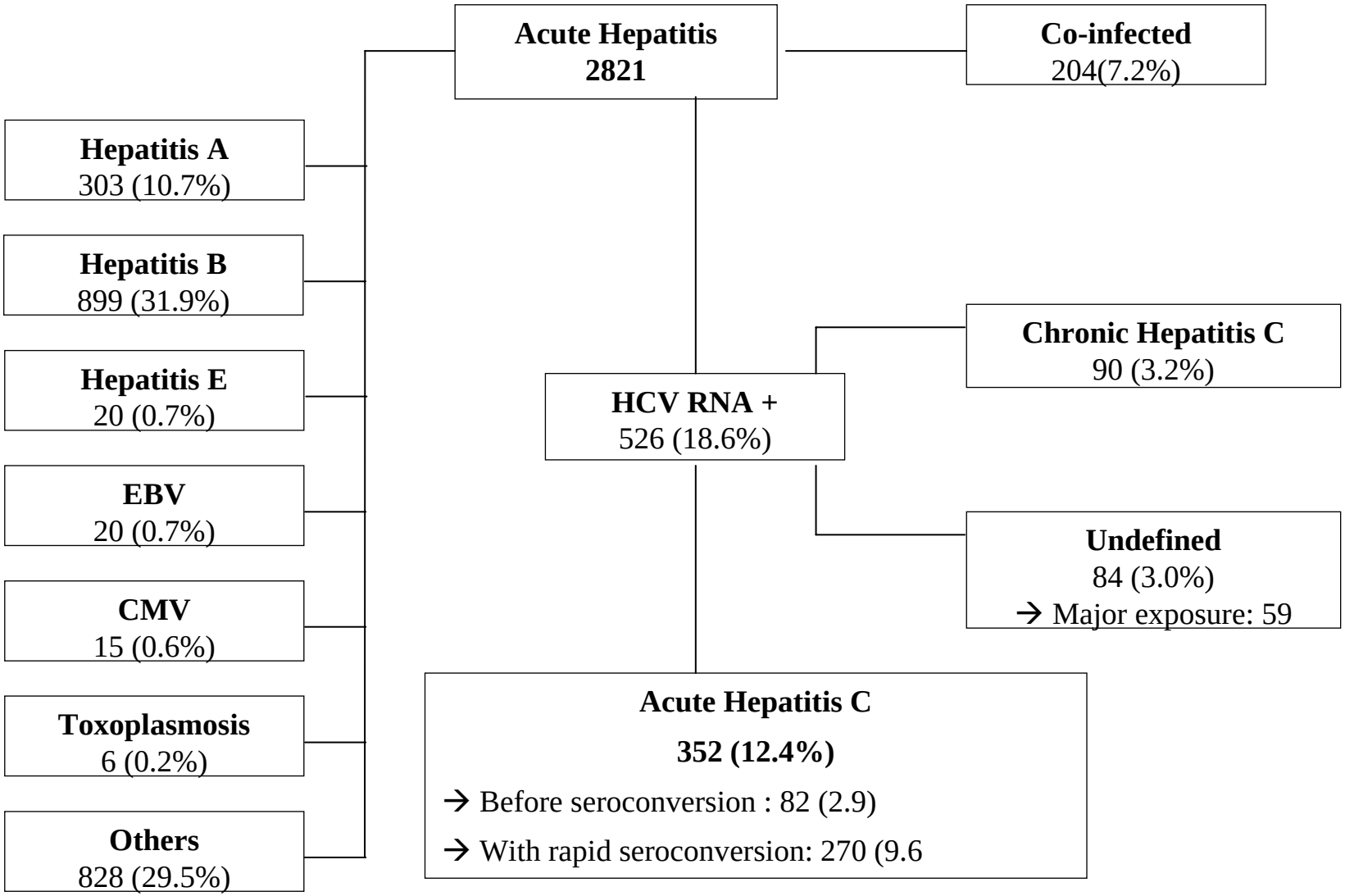
    → important for prevention.

- Challenge: finding acute hepatitis C cases.

Methods - Algorithm for diagnosis



Recruitment, Cairo Fever Hospitals, 2002-9



Methods

- Matched case-control study.
- Cases: acute hepatitis C cases recruited at Abassaia and Imbaba Fever Hospitals.
- Controls:
  - Patients with acute hepatitis A
  - Family controls of acute hepatitis C cases matched by age and sex to cases

Health care related risk factors, Greater Cairo, 2002-7.

	HCV cases* N=94 n (%)	HAV controls N=94 n (%)	Family controls N=94 N (%)	OR (95%CI) P value	
Hospital admission	15 (16.0)	3 (3.2)	5 (5.3)	3.8 (1.6-8.8)	0.002
Surgery	8 (8.5)	2 (2.1)	1 (1.1)	5.3 (1.4-20.1)	0.01
Stitches	21 (22.3)	6 (6.4)	3 (3.2)	5.1 (2.2-11.5)	<0.001
Intravenous injections	9 (9.6)	1 (1.1)	3 (3.2)	4.3 (1.3-14)	0.01
Intramuscular injections	13 (13.8)	12 (12.8)	18 (19.1)	0.8 (0.4-1.7)	0.63
Intravenous cannula	13 (13.8)	5 (5.3)	4 (4.3)	3.3 (1.3-8.5)	0.01
Endoscopy	1 (1.1)	0	0	---	---
Blood transfusion	0	0	0	---	---
Birth delivery	4 (14.3)	1 (3.6)	1 (3.6)	6.6 (0.7-60.9)	0.06
Cesarean section	3 (10.7)	0	0	---	0.05
Teeth extraction	12 (12.8)	11 (11.7)	5 (5.3)	1.5 (0.7-3.4)	0.3

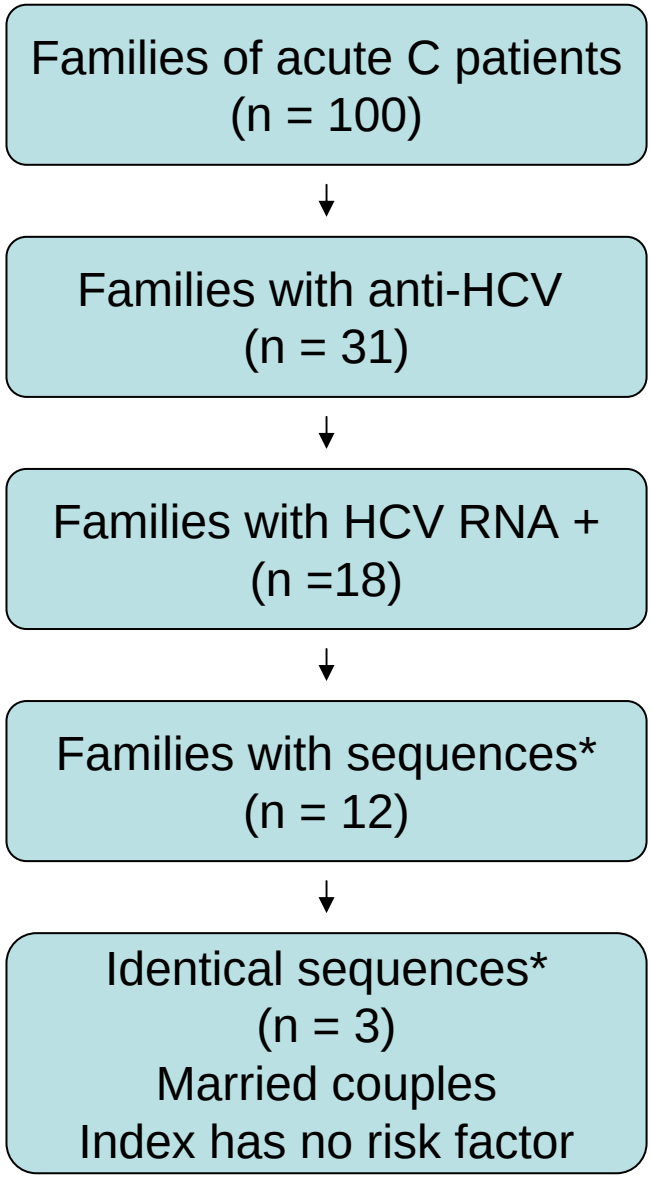
(Paez A et al. PLoS ONE 2009)

Factors independently associated with acute hepatitis C, multivariate analysis, Greater Cairo, 2002-7

	Adjusted OR (95% CI) N=275	P value
Intravenous injections	5.0 (1.2 – 20.2)	0.02
Medical stitches	4.2 (1.6 – 11.3)	0.004
Drug use		0.01
Never	1	
Sniffing	4.4 (1.6 – 12.1)	
Injecting	7.9 (1.4 – 43.5)	
Marriage duration		0.08
Single	1	
Less than 1 year	3.3 (1.1 – 9.9)	
One year or longer	1.8 (0.8 – 4.1)	
Illiteracy	3.9 (1.8 - 8.5)	0.001

(Paez A et al., PLoS ONE, 2009)

HCV intra-familial transmission



*330 base pairs NS5b

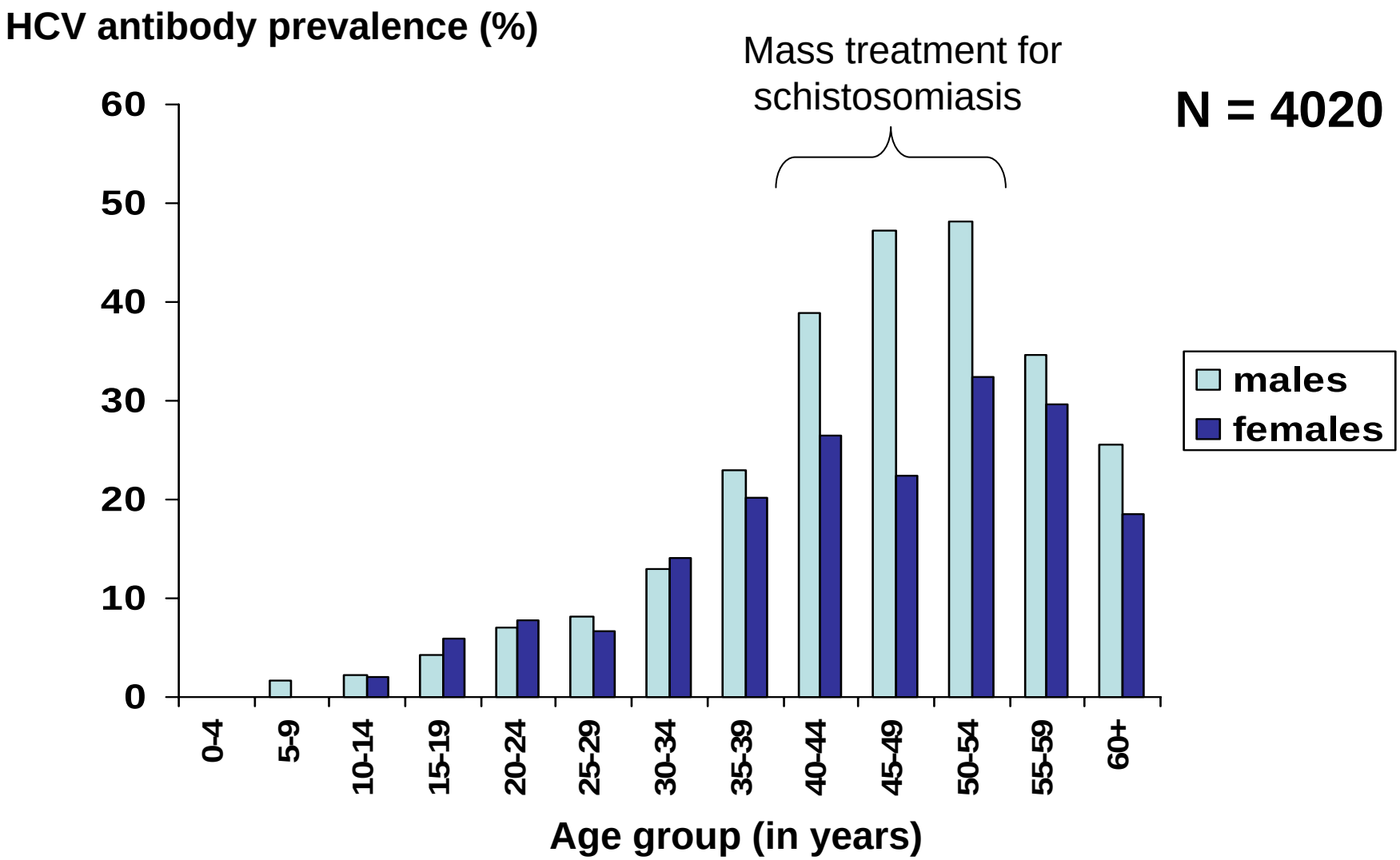
*>99.9% homology

Factors independently associated with acute hepatitis B 233 cases and 233 matched controls (age, sex), 2002- 2006

- **Men**
  - **Illiteracy (OR = 6.1, 95% CI = 2.8-13.1)**
  - **shaving at barbers (OR = 2.1, 95% CI = 1.1-3.9)**
  - **injecting drug use (OR = 3.4, 95% CI = 1.0-11.4)**
- **Women**
  - **Illiteracy (OR = 2.2, 95% CI = 1.0-5.0)**
  - **Recent (<1year) marriage (OR = 42.0, 95% CI = 3.8-463.9) compared to single women**
  - **Giving birth (OR = 3.7, 95% CI = 1.0-13.9)**

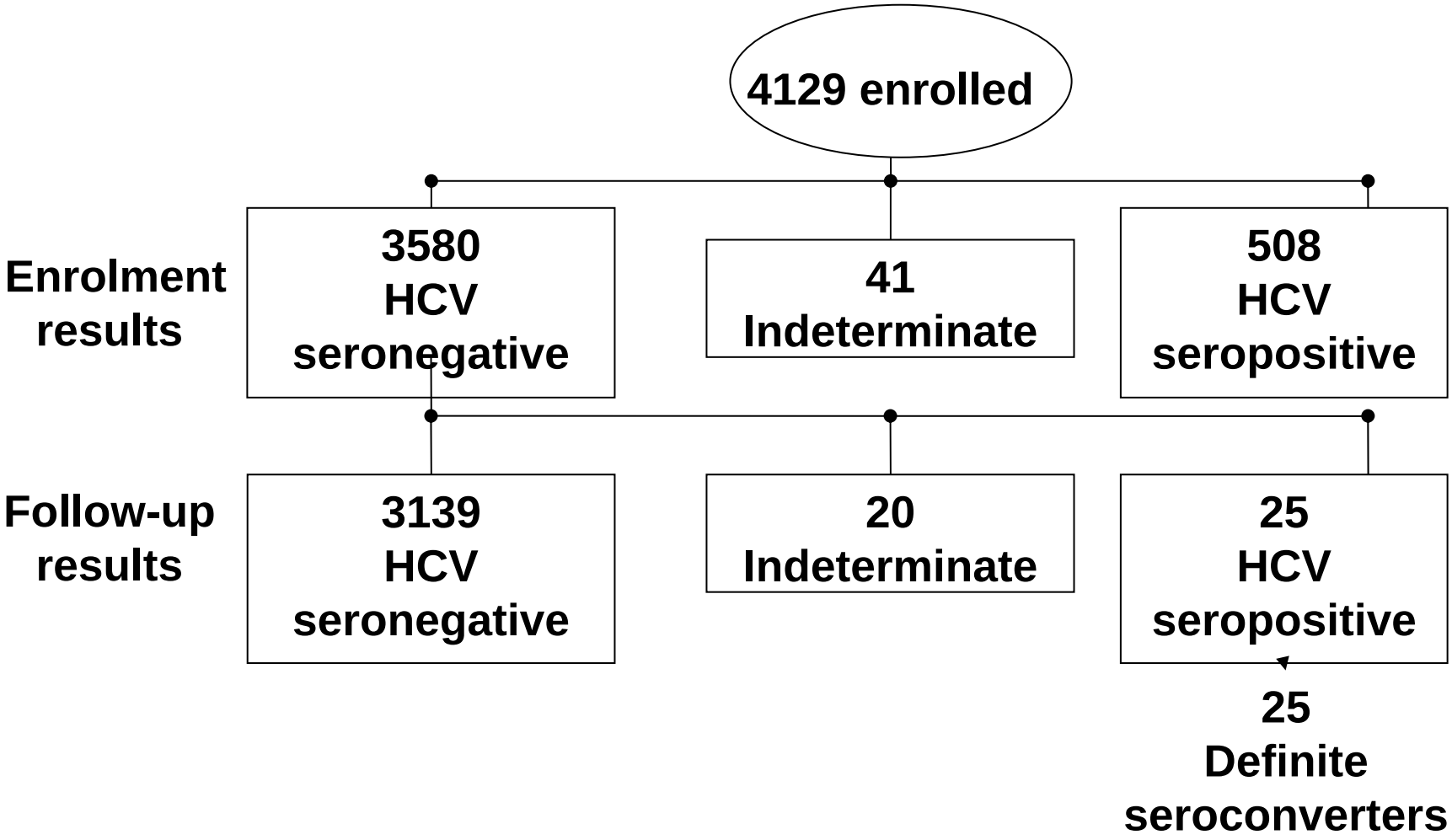
(Paez A et al, IJE, 2009)

Zwyat Razin cohort intake, 2002 (ANRS 1211 & 12107)



(Arafa et al, J Hepatol, 2005)

Follow-up in 2006



Incidence = 25/10578 person-years (PY) = 2.4 per 1000 PY

Conclusions (1)

- There is still substantial on-ongoing HCV transmission in Egypt.

	Prevalence	Incidence (per 1000 PY)
Assiout N=6000	24%	6.8
Menoufia N=4000	12%	2.4
Qualoubia N=4000	9%	0.8

Risk factors for incident HCV infections

- Only risk factor in nested case-control study: medical injections (OR = 3.3, 95%CI = 1.1- 9.8)

- Of 25 seroconverters, 17 were viremic, and 2 (12%) had HCV strains identical to someone living in the same household:
  - An 18-year old boy with same strain than his mother.
  - A 6-year old boy with same strain than siblings aged 11 and 13 years.

Genetic susceptibility to HCV infection

HCV intra-familial clustering
Zwyat Razin, 2002, n=4020 (ANRS 12107)

	Adjusted OR* HCV infection	% similar strains NS5b sequences
Husband-wife	2.2 (1.3 – 3.7)	1/16 = 6%
Father-child	3.4 (1.8 – 6.2)	2/16 = 12%
Mother-child	3.8 (2.5 – 5.8)	5/22 = 23%
Child-child	9.3 (4.9 – 17.6)	9/29 = 31%

*GEE2 models

(Plancoulaine et al, Gut, 2008)

Conclusions (2)

- Medical injections, infusions, catheters contribute to at least half of all new infections → infection control procedures in health care facilities need reinforcement.
- Social sciences studies using qualitative methods would be useful to better understand the circumstances around HCV infection in various contexts (hospitals, pharmacies, …).
- IV drug use in Cairo is an area that deserves attention, (also for HIV.)

Conclusions (3)

- Intra-familial transmission accounts for about 5-10% of all new infections.
- Routes of intrafamilial transmission are not yet understood; there is currently no basis to modify existing recommendations to prevent HCV transmission to other family members.
- Genetic predisposition to HCV infection may explain part of intra-familial clustering of infections, particularly when it involves children.

Acknowledgements

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- Population of Zwyat Razin, Menoufeya governorate.
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- ANRS.