

Réinfections par le VHC

« Sex, drugs & VHC »

Dr Laurent cotte

Service des Maladies Infectieuses

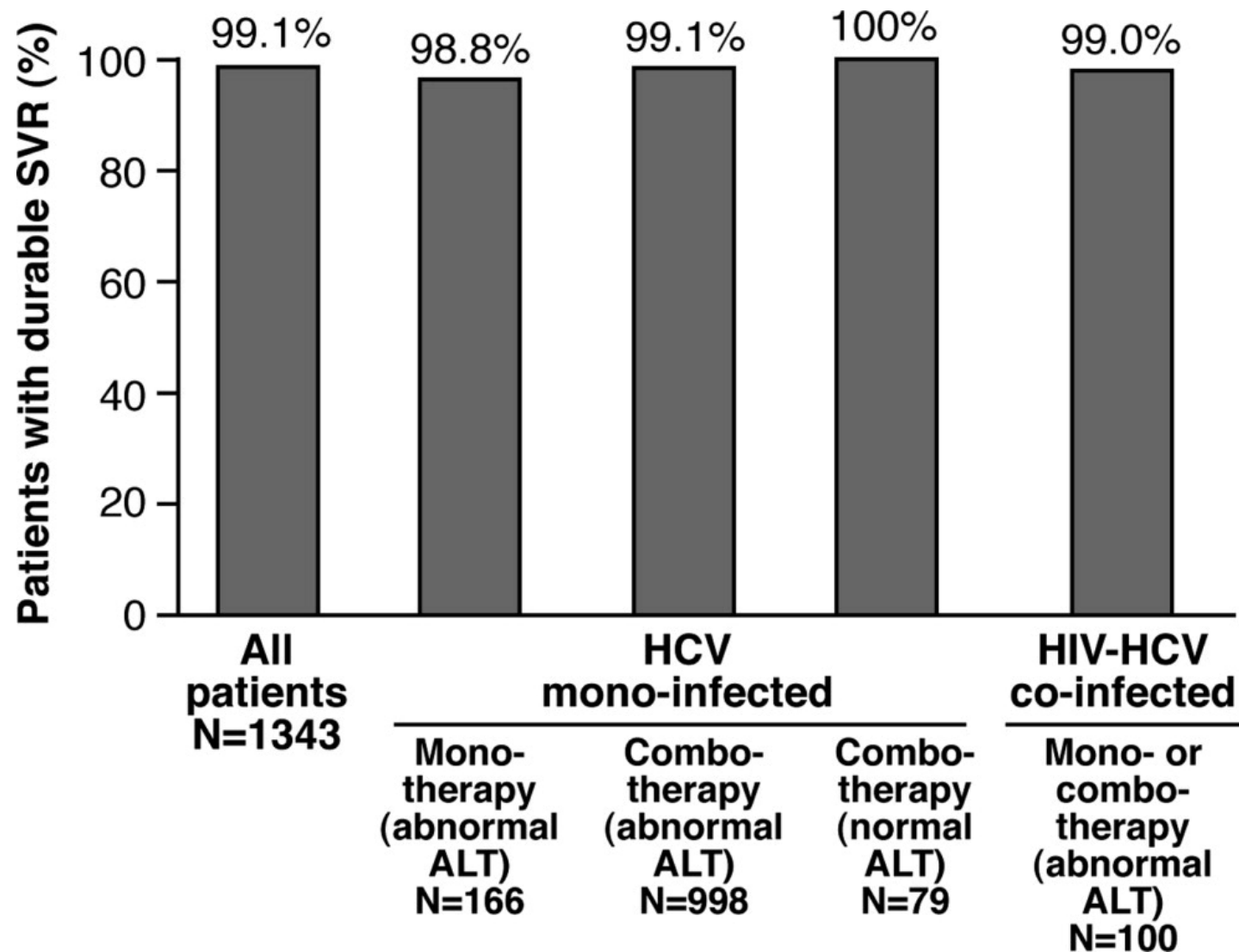
Hôpital de la Croix-Rousse

Définitions

- Coinfection : infection initiale avec > 1 virus génétiquement différents
- Surinfection : infections successives avec > 1 virus génétiquement différents
- Réinfection : ARN-VHC+ après guérison spontanée ou post-traitement
 - Infection par un nouveau génotype après guérison d'une 1^{ère} infection
 - Infection par un virus différent dans le même génotype (analyse phylogéniques)
 - Réinfection par le même virus ?
- Rechute tardive : re-émergence du même virus > 24 semaines post-traitement

A Sustained Virologic Response Is Durable in Patients With Chronic Hepatitis C Treated With Peginterferon Alfa-2a and Ribavirin

MARK G. SWAIN,* MING-YANG LAI,† MITCHELL L. SHIFFMAN,§ W. GRAHAM E. COOKSLEY,|| STEFAN ZEUZEM,¶
DOUGLAS T. DIETERICH,# ARMAND ABERGEL,** MÁRIO G. PESSÔA,†† AMY LIN,‡,§§ ANDREAS TIETZ,|||
EDWARD V. CONNELL,§§ and MOISÉS DIAGO¶¶¶

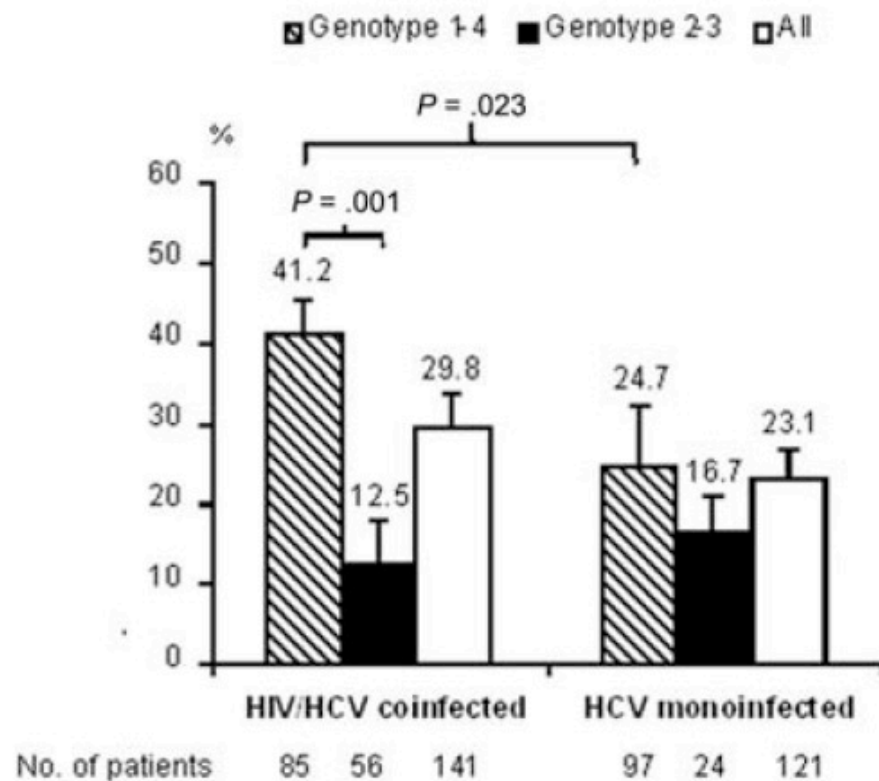


Rate and Timing of Hepatitis C Virus Relapse after a Successful Course of Pegylated Interferon plus Ribavirin in HIV-Infected and HIV-Uninfected Patients

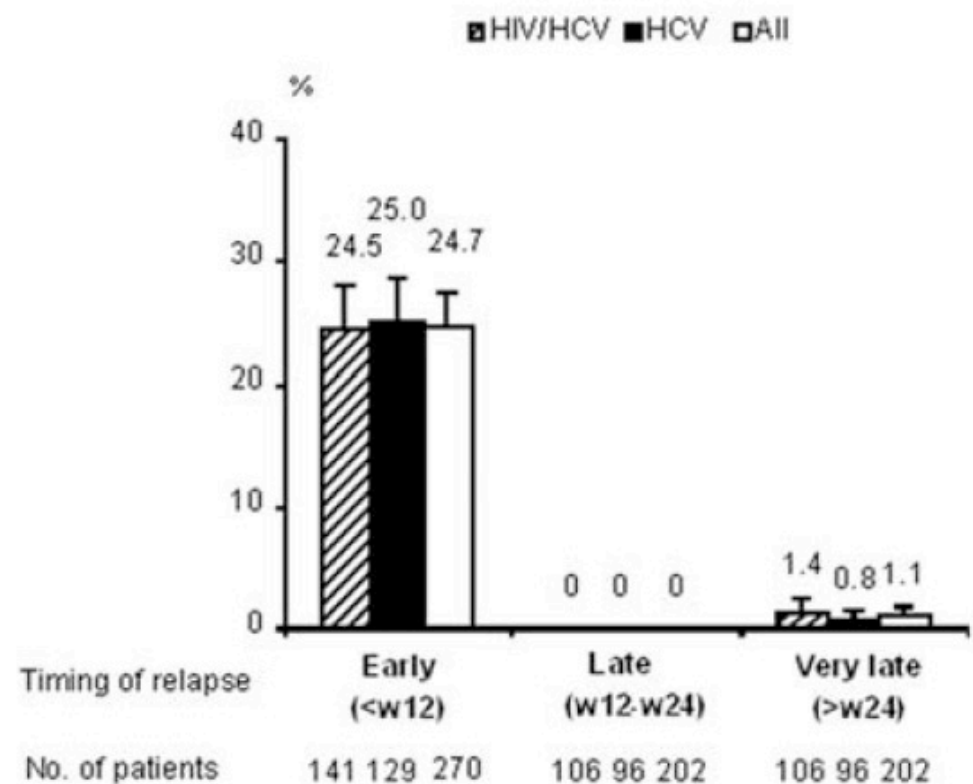
José Medrano,¹ Pablo Barreiro,¹ Salvador Resino,⁴ Paula Tuma,¹ Violeta Rodríguez,¹ Eugenia Vispo,¹ Pablo Labarga,¹ Antonio Madejón,^{1,2} Javier García-Samaniego,² Inmaculada Jiménez-Nácher,³ Luz Martín-Carbonero,¹ and Vincent Soriano¹

Clinical Infectious Diseases 2009;49:1397–1401

A

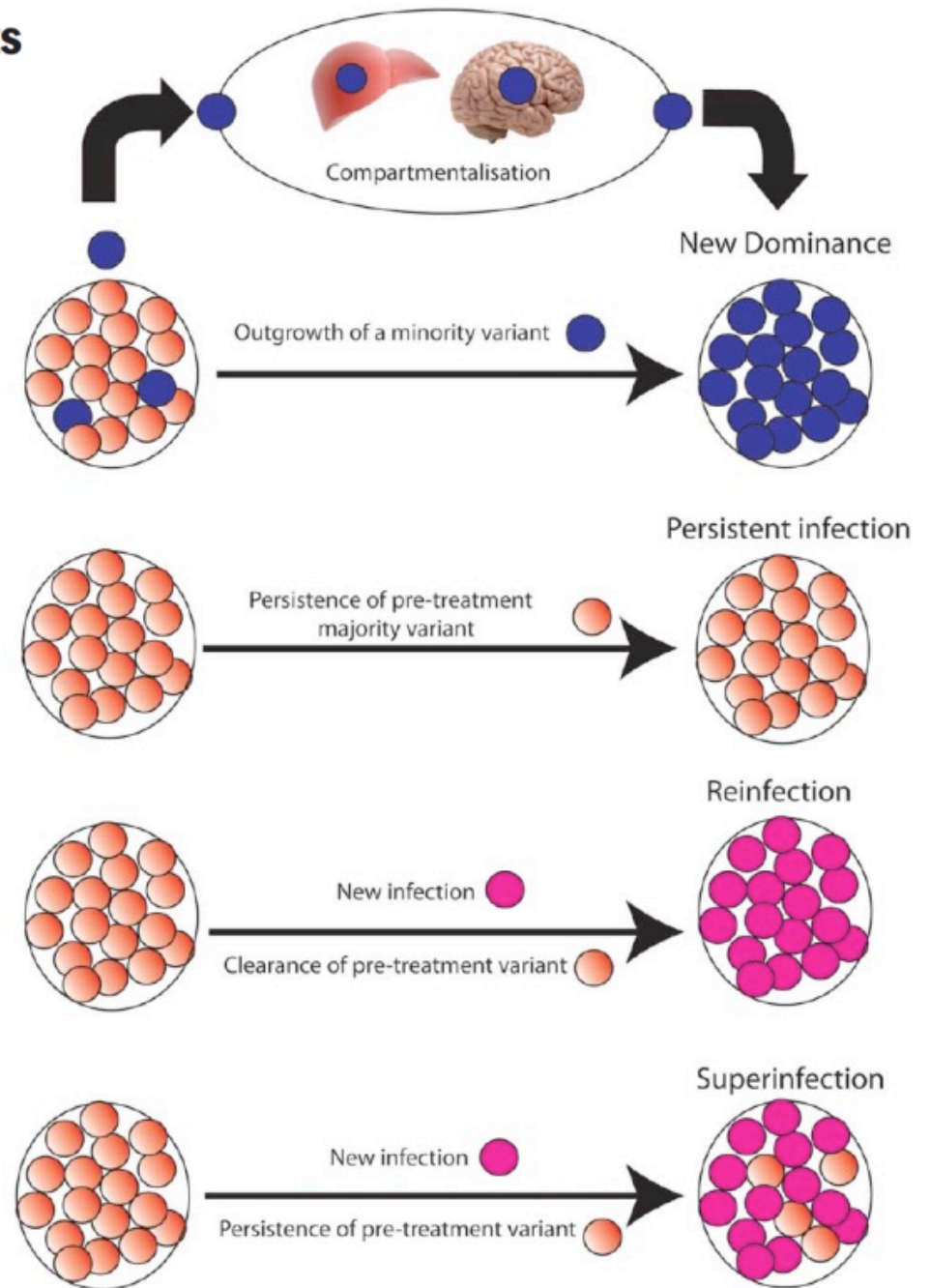


B



Next-Generation Sequencing Sheds Light on the Natural History of Hepatitis C Infection in Patients Who Fail Treatment

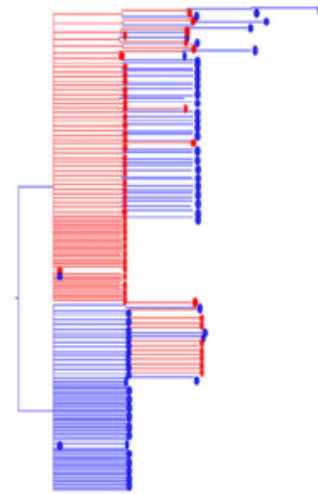
Tamer Abdelrahman,¹ Joseph Hughes,¹ Janice Main,² John McLauchlan,¹ Mark Thursz,² and Emma Thomson^{1,2}



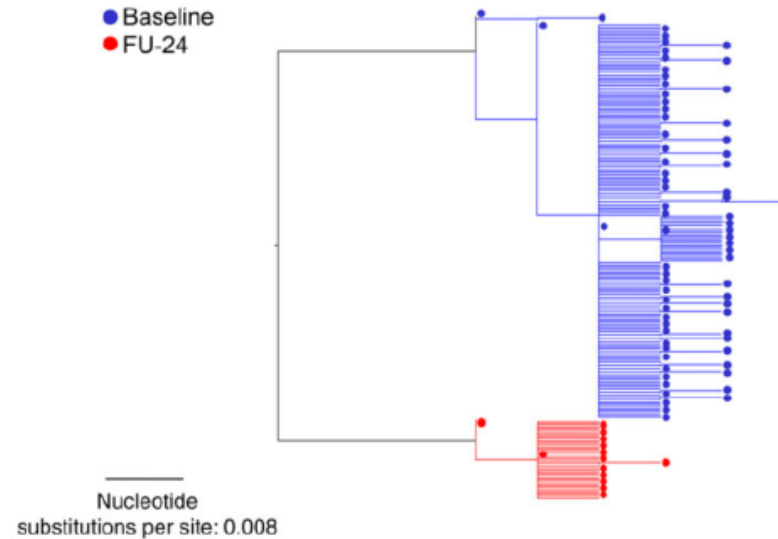
Late Relapse Versus Hepatitis C Virus Reinfection in Patients With Sustained Virologic Response After Sofosbuvir-Based Therapies

Christoph Sarrazin,¹ Vasily Isakov,² Evguenia S. Svarovskaia,³ Charlotte Hedskog,³ Ross Martin,³ Krishna Chodavarapu,³ Diana M. Brainard,³ Michael D. Miller,³ Hongmei Mo,³ Jean-Michel Molina,⁵ and Mark S. Sulkowski⁴

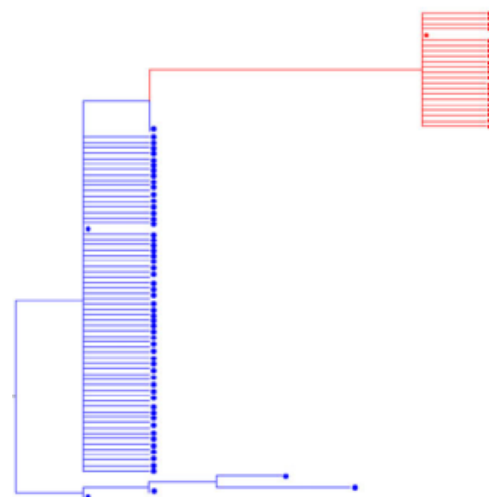
A Late-Relapse: Patient 9 (GT3a)



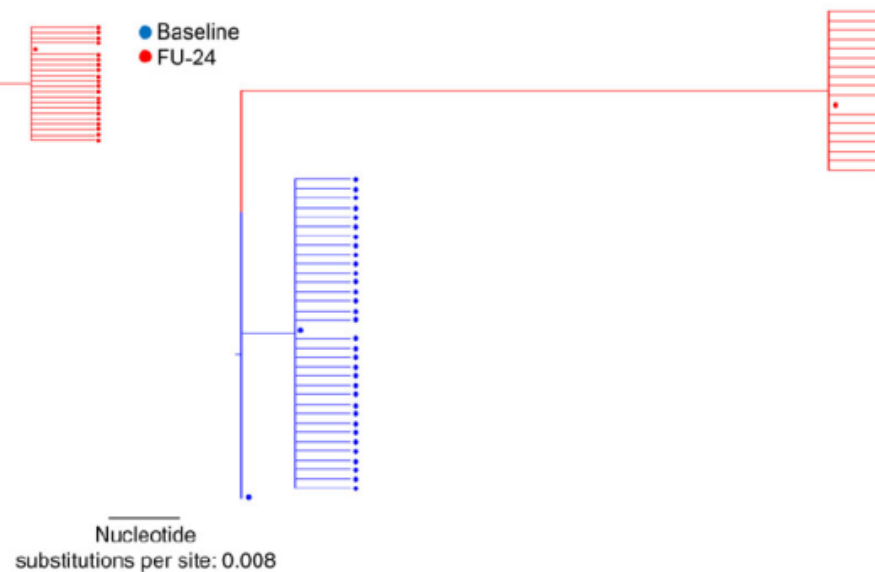
B Reinfection: Patient 3 (GT1a)



C Reinfection: Patient 7 (GT3a)



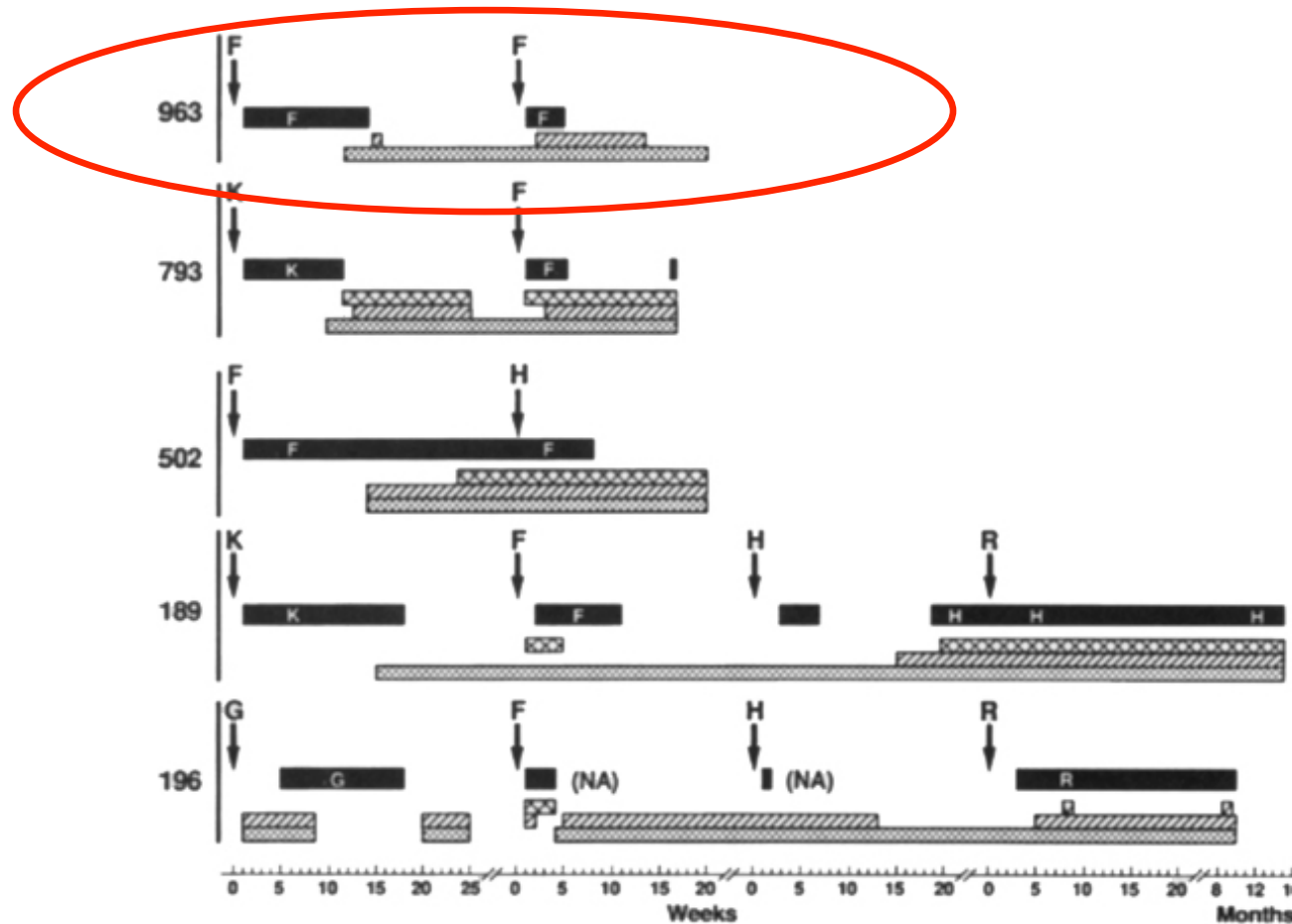
Reinfection: Patient 6 (GT1a)



Lack of Protective Immunity Against Reinfection with Hepatitis C Virus



Patrizia Farci,* Harvey J. Alter, Sugantha Govindarajan, Doris C. Wong, Ronald Engle, Richard R. Lesniewski, Isa K. Mushahwar, Suresh M. Desai, Roger H. Miller, Norio Ogata, Robert H. Purcell



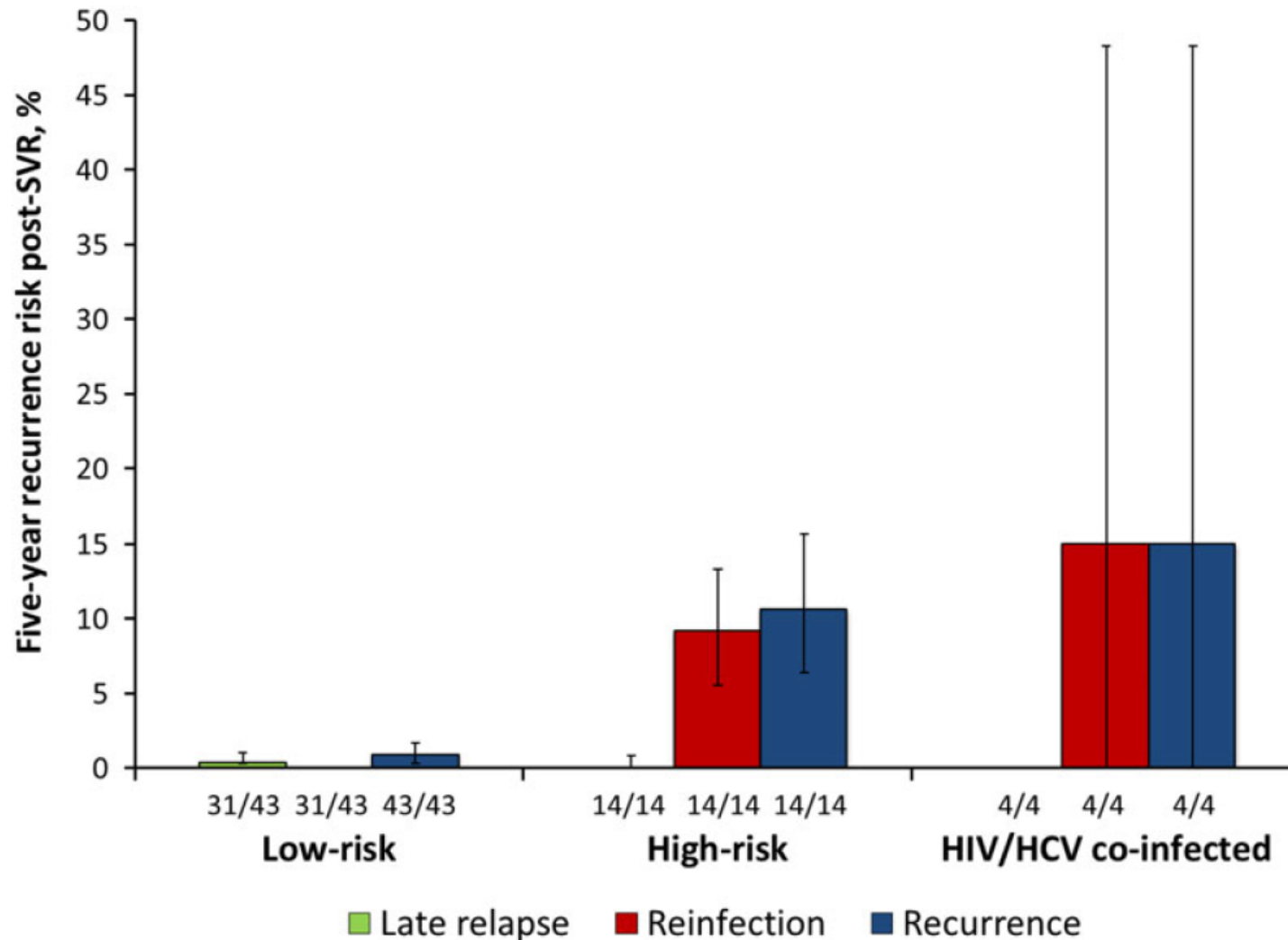
Hepatitis C virus clearance, reinfection, and persistence, with insights from studies of injecting drug users: towards a vaccine

Jason Grebely, PhD, Prof Maria Prins, PhD, Prof Margaret Hellard, PhD, Andrea L Cox, PhD, William O Osburn, PhD, Georg Lauer, MD, Kimberly Page, PhD, Prof Andrew R Lloyd, PhD, and Prof Gregory J Dore, PhD on behalf of the International Collaboration of Incident HIV and Hepatitis C in Injecting Cohorts (InC³)

	Study populations	Number of new infections during follow-up	Median follow-up (years)	Incidence rate per 100 person-years	Crude incidence rate ratio	Adjusted ratio (95% CI)	p value	Median HCV RNA testing interval for patients previously infected (months)*	Clearance of reinfection in patients whose infection had previously cleared†	Reinfection in prevalent or incident cases?
Mehta ¹²	Not infected (n=164) vs HCV clearance (n=98)	35 vs 12	2.4 vs 2.1	8.6 vs 5.4	0.63	0.45 (0.23–0.88)‡	0.02	6.3 (6)	6 of 9 (67%)‡	Prevalent
Grebely ¹³	Not infected (n=926) vs HCV clearance (n=152)	172 vs 14	2.8 vs 5.2	8.1 vs 1.8	0.22	0.23 (0.10–0.51)§	<0.001	15.6	4 of 14 (29%)	Prevalent
Micallef ¹⁴	Not infected (n=423) vs HCV clearance (n=18)	114 vs 13	1.0 vs 1.2	17.0 vs 42.0	2.47	1.1¶	0.80	5.0 (6)	3 of 7 (43%)	Incident
Aitken ¹⁵	Not infected (n=55) vs HCV clearance (n=50)	10 vs 23	NA	15.5 vs 46.8	3.02	2.54 (1.11–5.78)‡	0.027	3.8 (3)	9 of 22 (41%)	Prevalent and incident
van de Laar ¹⁷	Not infected (n=168)// vs HCV clearance (n=24)	58 vs 9	3.6 vs 10.5	6.7 vs 9.9	1.5	NA	NA	7.3 (4–6)	3 of 9 (33%)	Incident
Page ¹⁸	Not infected (n=380) vs HCV clearance (n=27)	132 vs 7	NA	26.7 vs 24.6	0.92	NA	NA	3.0 (3)	7 of 7 (100%)	Incident
Osburn ¹⁰	Not infected (n=179)** vs HCV clearance (n=22)	62 vs 11	NA	27.2 vs 30.1	1.11	NA	NA	1.0 vs 1.0 (1)	10 of 12 (83%)	Incident
Currie ¹⁶	HCV clearance (n=29)	0	5.5	0.0	NA	NA	NA	NA (6)	0 of 29	Prevalent
Grebely ¹⁹	HCV clearance (n=30)	2	1.1	6.1	NA	NA	NA	3.0 (3)	2 of 2 (100%)	Incident

Risk of Late Relapse or Reinfection With Hepatitis C Virus After Achieving a Sustained Virological Response: A Systematic Review and Meta-analysis

Bryony Simmons,¹ Jawaad Saleem,¹ Andrew Hill,² Richard D. Riley,³ and Graham S. Cooke¹



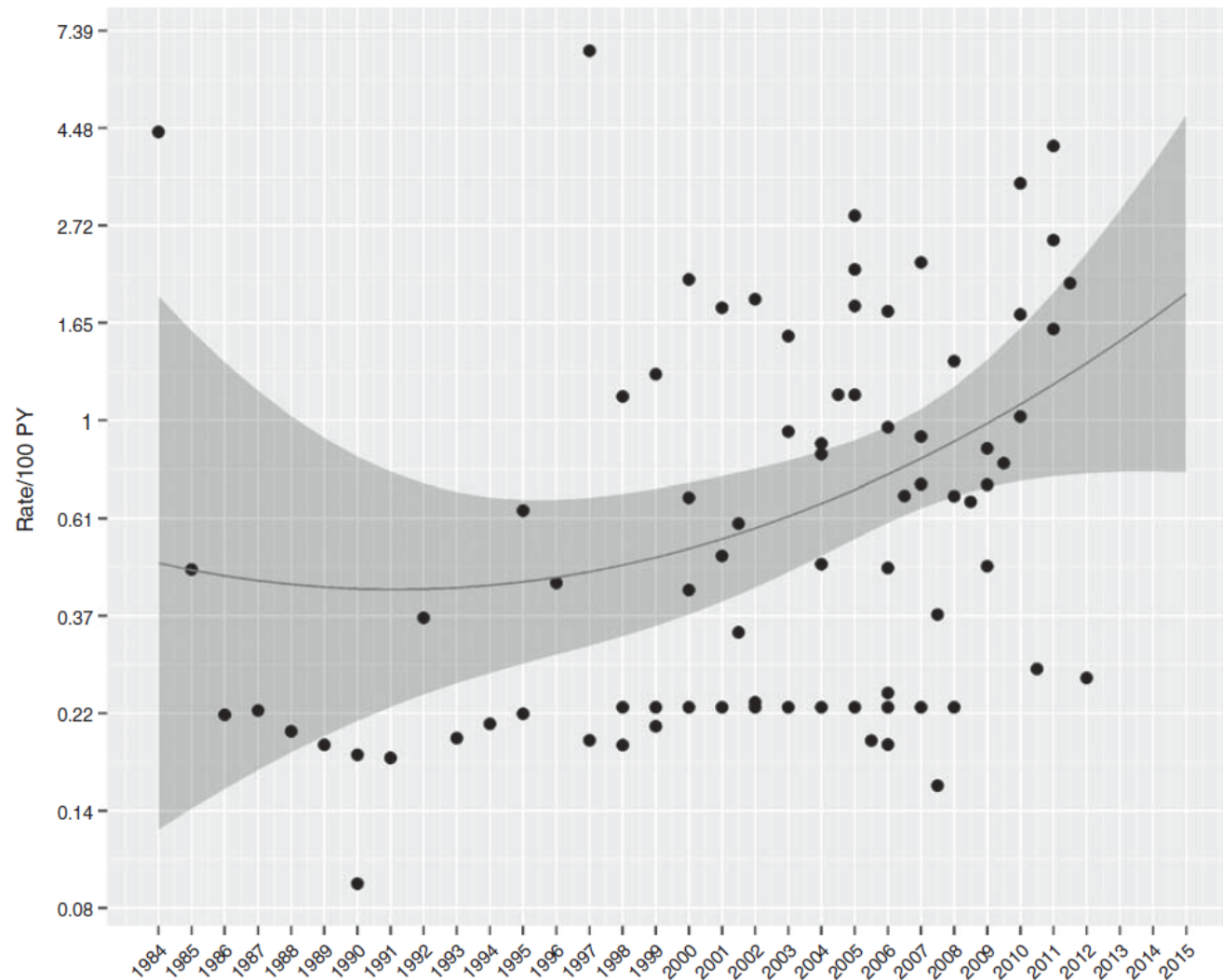
Sexual Transmission of Hepatitis C Virus Among Monogamous Heterosexual Couples: The HCV Partners Study

Norah A. Terrault,¹ Jennifer L. Dodge,¹ Edward L. Murphy,^{1,2} John E. Tavis,³ Alexi Kiss,³ T. R. Levin,⁴ Robert G. Gish,⁵ Michael P. Busch,^{1,2} Arthur L. Reingold,⁶ and Miriam J. Alter⁷

- 500 couples hétérosexuels. 1 partenaire VHC+
- Prévalence VHC chez l'autre partenaire 4% (n=20)
- 9 génotype concordant. dont 3 isolats apparentés
- 8 377 PA FU : Incidence **0.07 % / an** (1/190 000 RS)

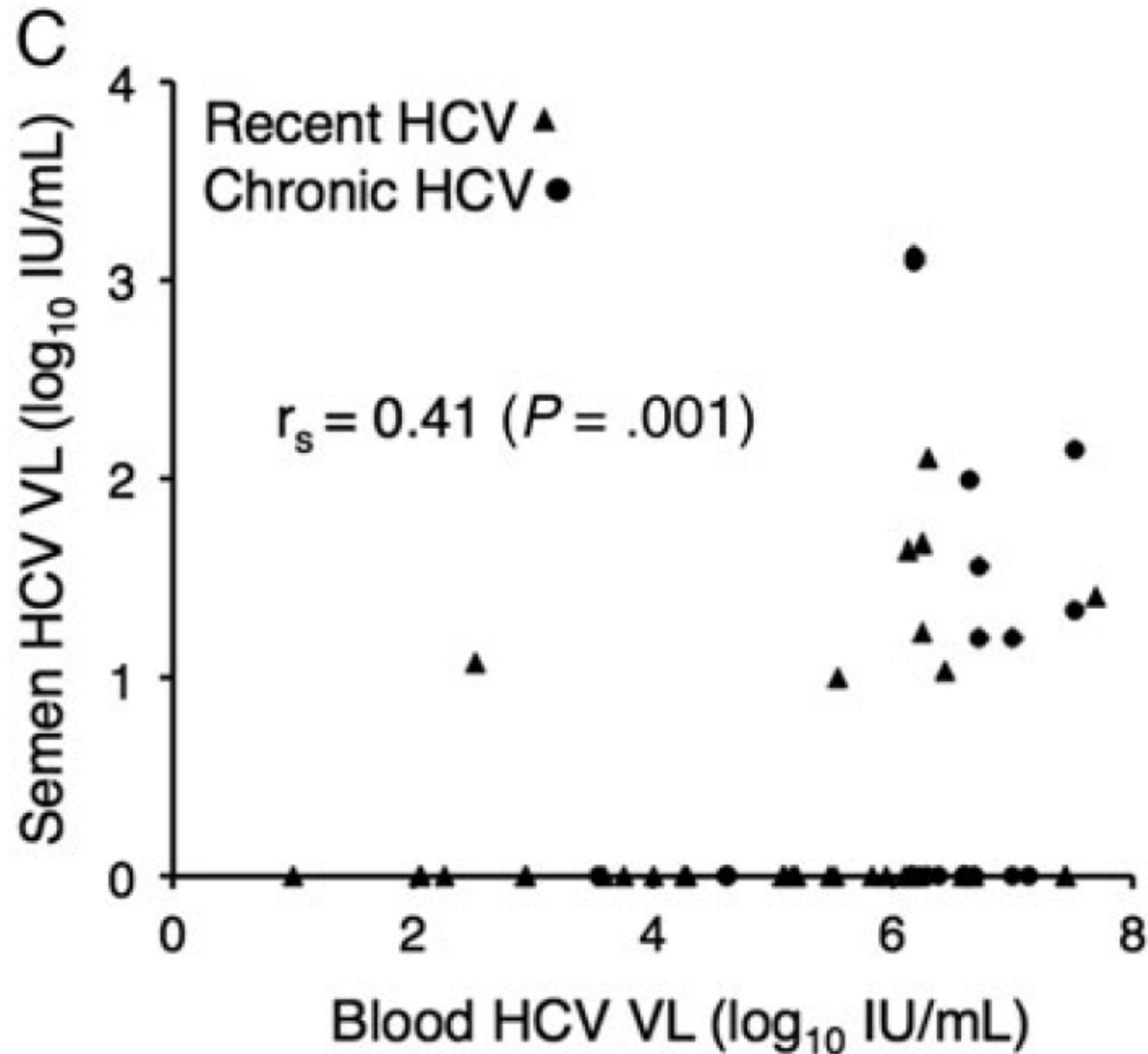
Incidence of sexually transmitted hepatitis C virus infection in HIV-positive MSM: a systematic review and meta-analysis

Holly Hagan, Ashly E. Jordan, Joshua Neurer and Charles M. Cleland



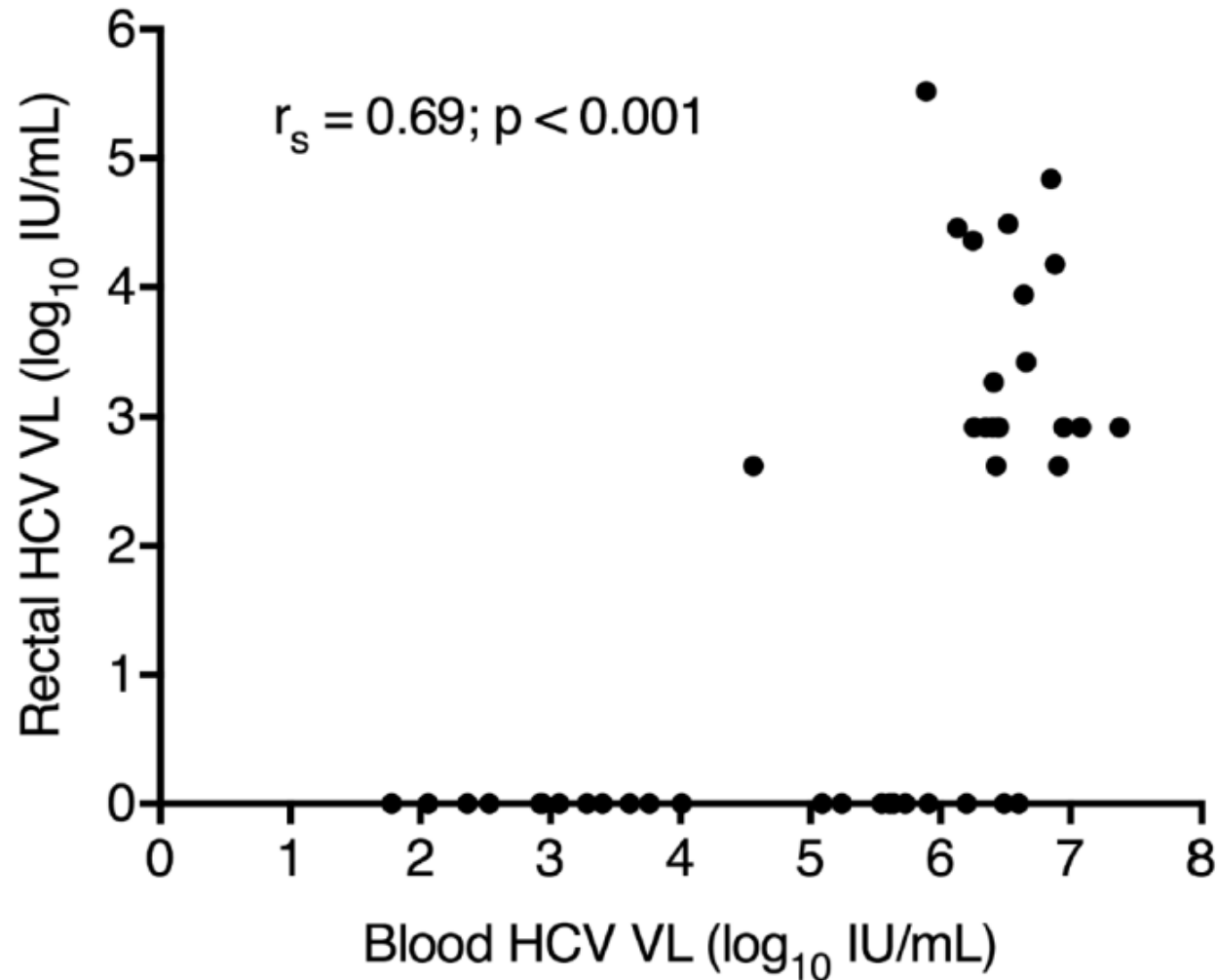
Shedding of Hepatitis C Virus in Semen of Human Immunodeficiency Virus-Infected Men

Samuel S. Turner,¹ Sara Gianella,² Marcus J-S. Yip,¹ Wouter O. van Seggelen,¹ Robert D. Gillies,¹ Andrew L. Foster,¹ Zachary R. Barbati,¹ Davey M. Smith,² and Daniel S. Fierer¹



Shedding of Hepatitis C Virus Into the Rectum of HIV-infected Men Who Have Sex With Men

Andrew L. Foster,¹ Michael M. Gaisa,¹ Rosanne M. Hijdra,¹ Samuel S. Turner,¹ Tristan J. Morey,¹ Karen B. Jacobson,¹ and Daniel S. Fierer¹



Trouble with Bleeding: Risk Factors for Acute Hepatitis C among HIV-Positive Gay Men from Germany—A Case-Control Study

Axel J. Schmidt^{1*}, Jürgen K. Rockstroh², Martin Vogel², Matthias An der Heiden¹, Armin Baillot³, Ivanka Krznicaric⁴, Doris Radun¹

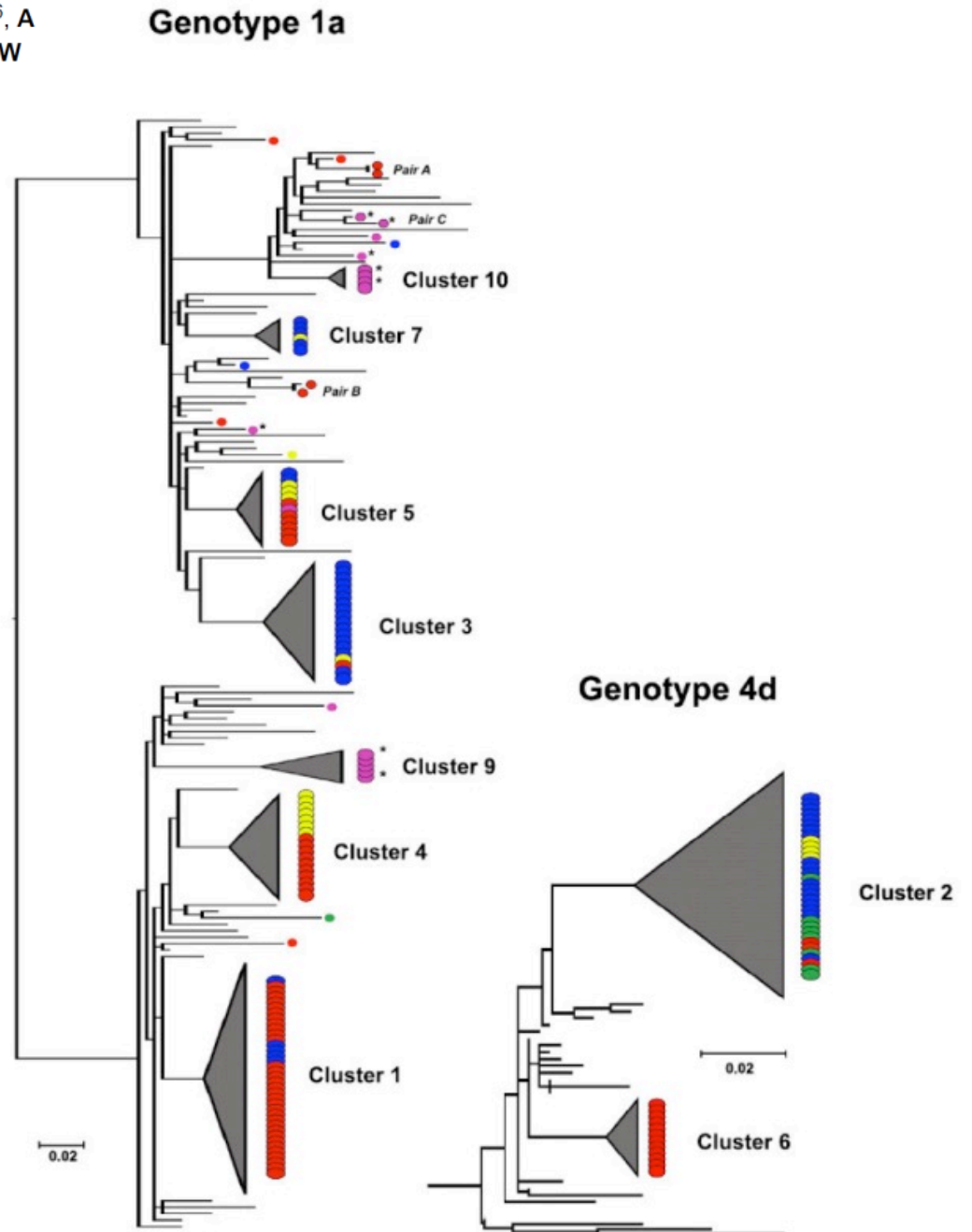
	Univariée		Multivariée	
	OR	<i>p</i>	OR	<i>p</i>
RANP insertif	2.89	0.019	-	0.347
RANP réceptif	2.25	0.062	-	0.759
IST (NG, CT, TP)	2.78	0.02	-	0.211
Partenaire VIH+	2.94	0.029	-	0.986
Sexe de groupe	5.4	0.007	3.5	0.084
Inhibiteurs PDE-5	3.62	0.008	-	0.557
Sex toys	3.13	0.0028	-	0.588
RA sanglants	5.53	0.029	6.19	0.032
Fisting réceptif sans gants	7.53	0.001	5.71	0.011
Drogues nasales	4.27	0.004	3.25	0.04

Evidence of a large, international network of international hepatitis C virus transmission in HIV-positive men who have sex with men

T van de Laar¹, O Pybus², S Bruisten¹, D Brown³, M Nelson⁴, S Bhagani⁵, M Vogel⁶, A Baumgarten⁷, ML Chaix⁸, M Fisher⁹, H Gótz¹⁰, G Matthews¹¹, S Neifer⁷, P White¹², W Rawlinson¹², S Pol¹³, J Rockstroh⁶, R Coutinho^{1,14}, G Dore¹¹, G Dusheiko³, and M Danta^{3,16}

Gastroenterology. 2009 May ; 136(5): 1609–1617.

Figure 1. NS5B phylogenetic trees of HCV genotypes 1a (left) and 4d (right)
 Monophyletic clusters are shaded, country of origin coded: (●) England, (●) Netherlands, (●) Germany, (●) France, (●) Australia. Australian MSM with reported IDU are marked IDU*



Sexually transmitted hepatitis C virus superinfection in HIV/hepatitis C virus co-infected men who have sex with men

Jade Ghosn^{a,b}, Vincent Thibault^c, Constance Delaugerre^a, H el ene Fontaine^d, Olivier Lortholary^e, Christine Rouzioux^a, Stanislas Pol^d and Marie-Laure Chaix^a

AIDS 2008, Vol 22 No 5

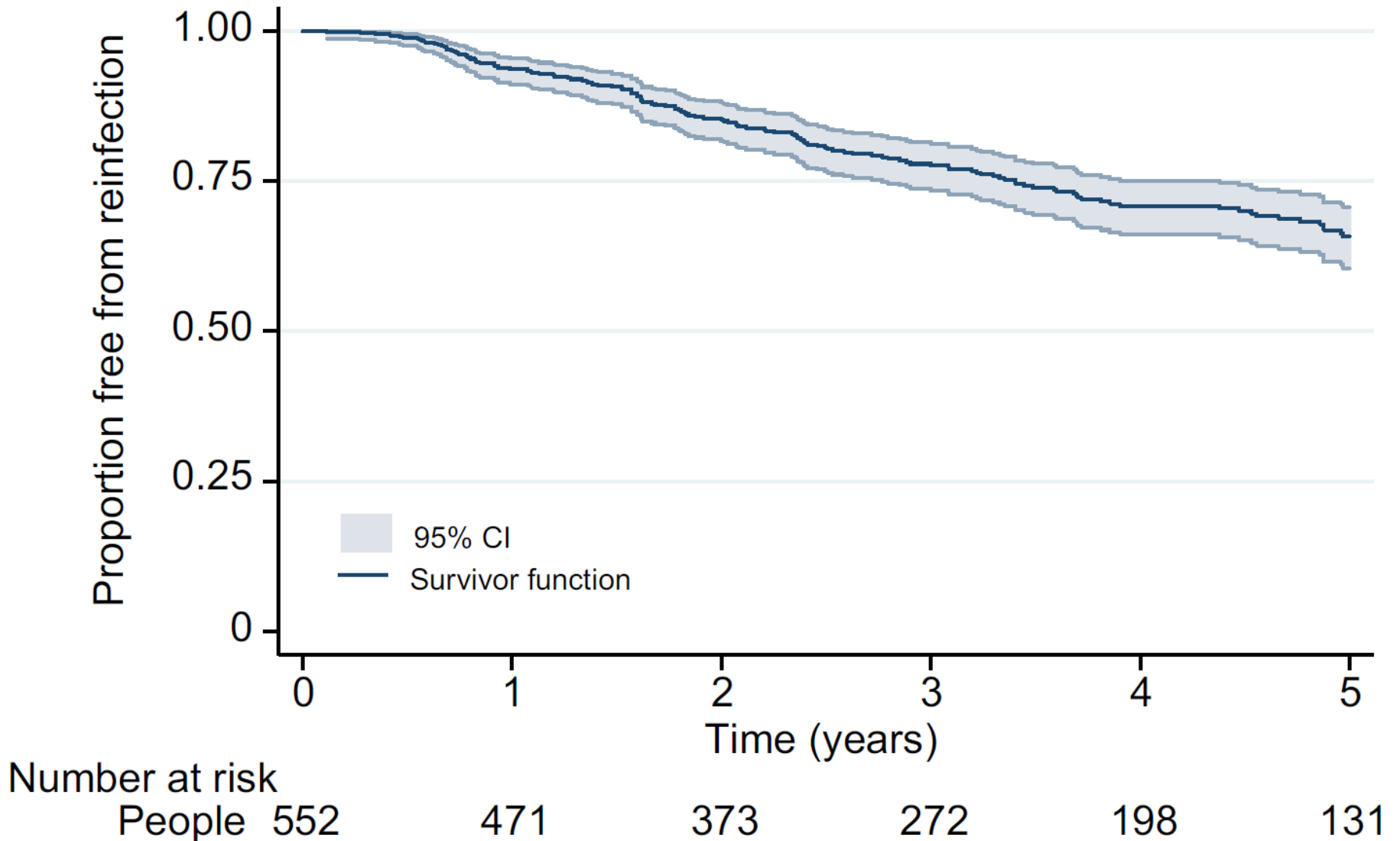
Sexually transmitted HCV infection and reinfection in HIV-infected homosexual men

Infections et r einfections d'origine sexuelle par le VHC chez des patients homosexuels infect es par le VIH

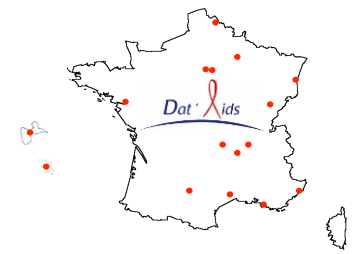
L. Cotte^{a,*}, P. Chevallier Queyron^{b,c}, I. Schlienger^a, M.-A. Trabaud^c, C. Brochier^a, P. Andr e^{c,e,f}, F. Zoulim^{a,b,d}

HCV reinfection incidence and spontaneous clearance rates in HIV-positive men who have sex with men in Western Europe

Patrick Ingiliz^{1,*†}, Thomas C. Martin^{2,†}, Alison Rodger³, Hans-Jürgen Stellbrink⁴, Stefan Mauss⁵, Christoph Boesecke⁶, Mattias Mandorfer⁷, Julie Bottero⁸, Axel Baumgarten¹, Sanjay Bhagani³, Karine Lacombe^{8,9}, Mark Nelson^{2,10}, Jürgen K. Rockstroh⁶, NEAT study group

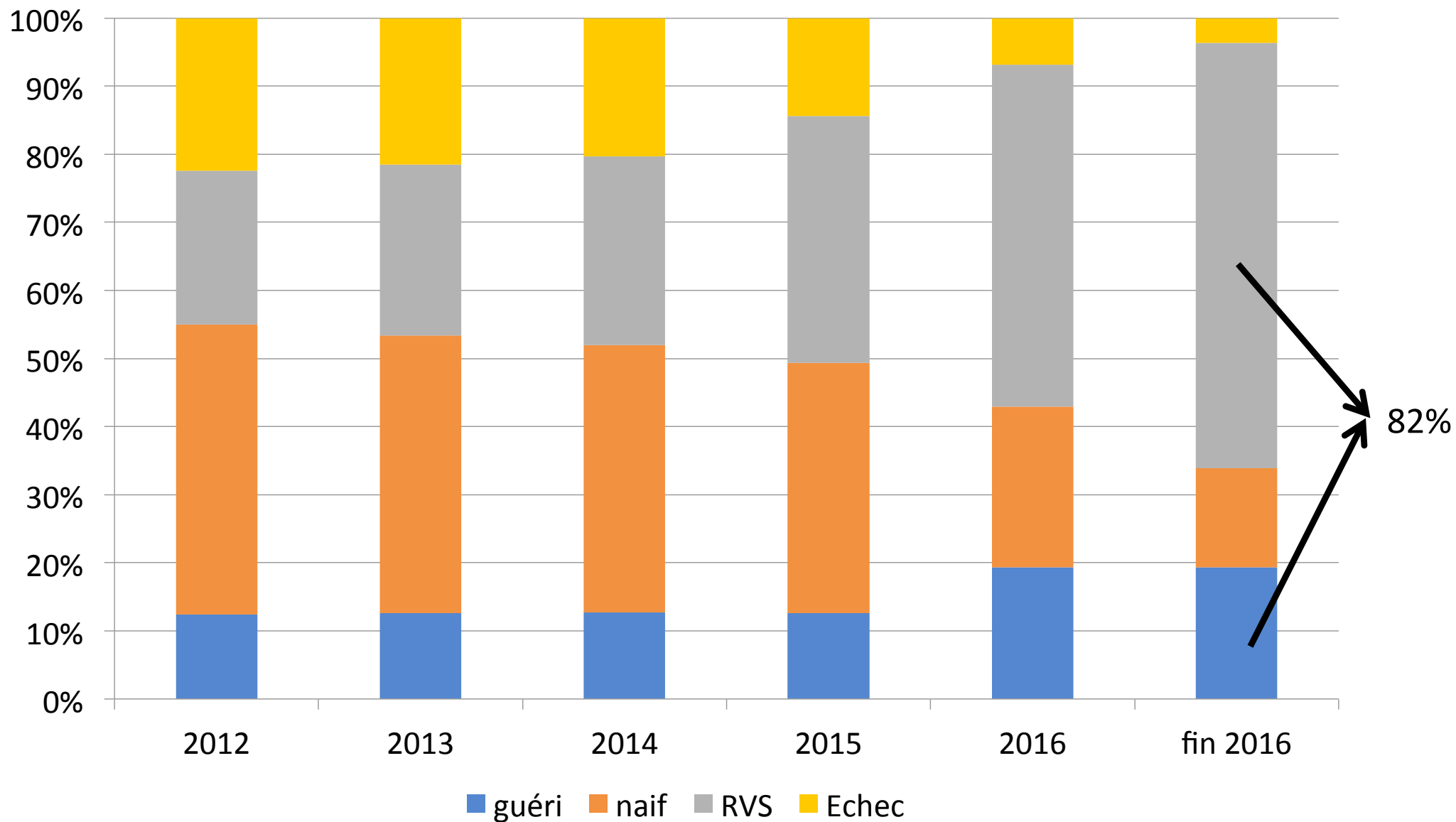
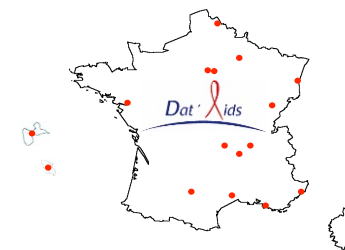


Caractéristiques de la population coinfectée en France

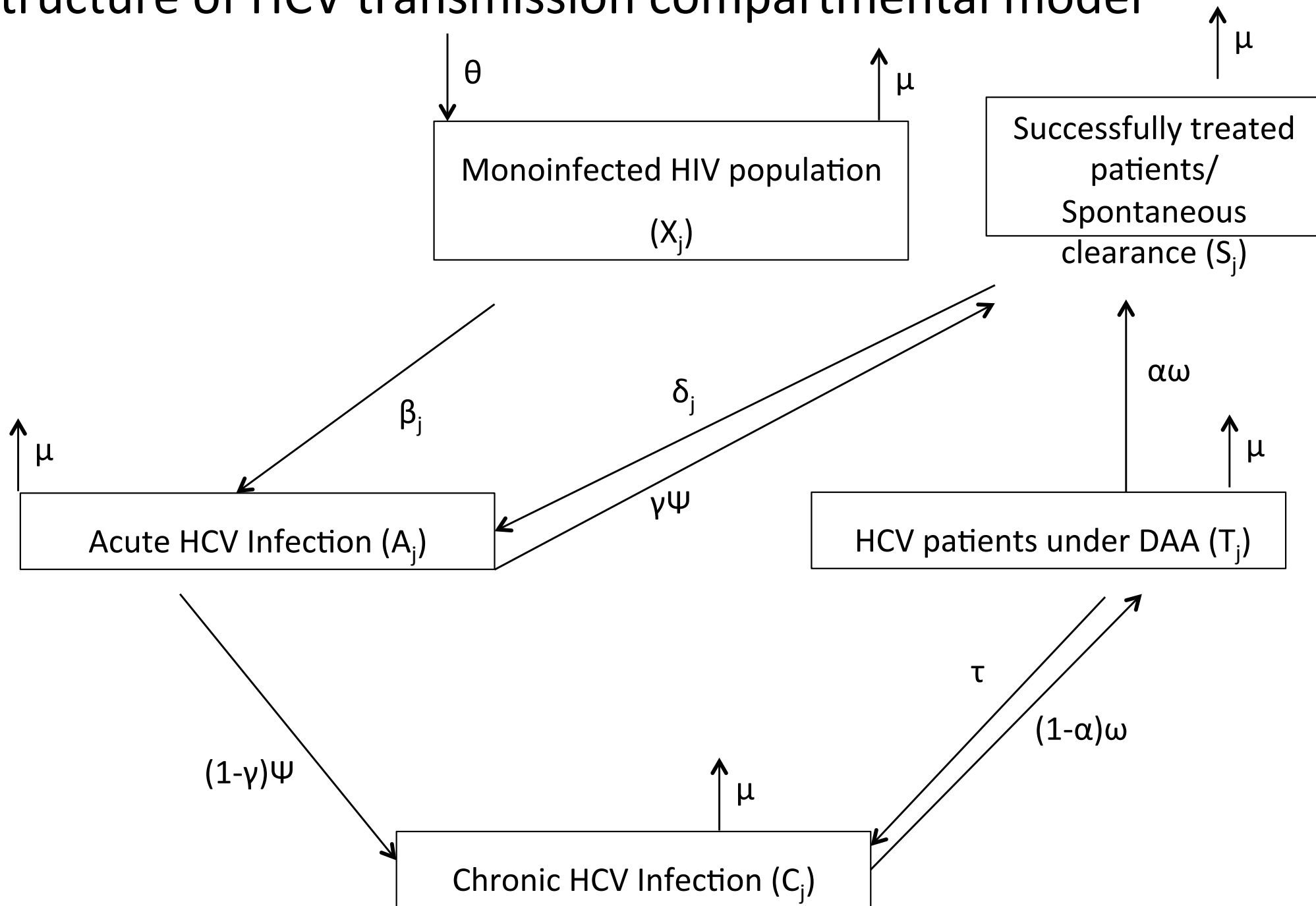


- Fort niveau d'engagement des VIH+ dans le soin (>80%) ¹
- Prévalence VHC en diminution constante depuis 15 ans (14.2% en 2016) ²
- Faible prévalence du VHC / nouveaux VIH : 2.9% entre 2012 et 2015 (donc faible incidence dans l'épidémie cachée)
- Faible incidence du VHC dans la plupart des groupes à risque. y compris anciens IVDU (90% IVDU VIH+ = anciens usagers)
- Incidence VHC élevée chez HSH. mais risque hétérogène en fonction des pratiques : notion de HSH à haut risque
- Taux d'initiation de traitement VHC élevé (pas de critère de fibrose) : 29.6% en 2015. 42.5% en 2016
- Patients virémiques = 18.2% fin 2016

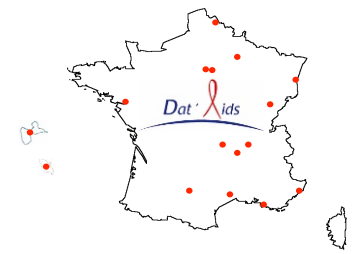
Evolution du statut des patients VIH-VHC en France



Structure of HCV transmission compartmental model



Modeling HIV-HCV epidemiology

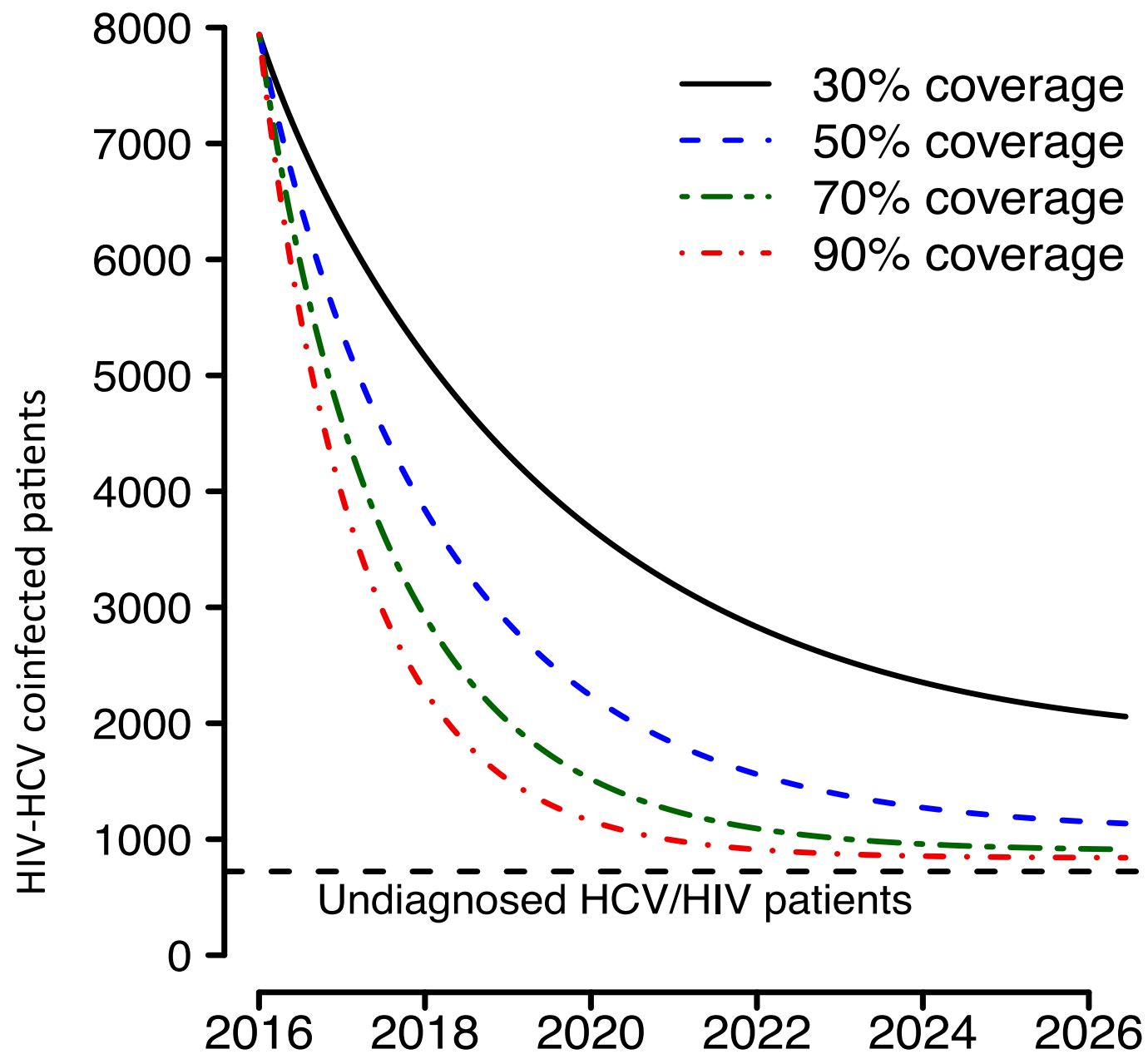


LR MSM 82%	HR MSM 18%	♂ IVDU	♂ heterosexual	♂ other
		♀ IVDU	♀ heterosexual	♀ other

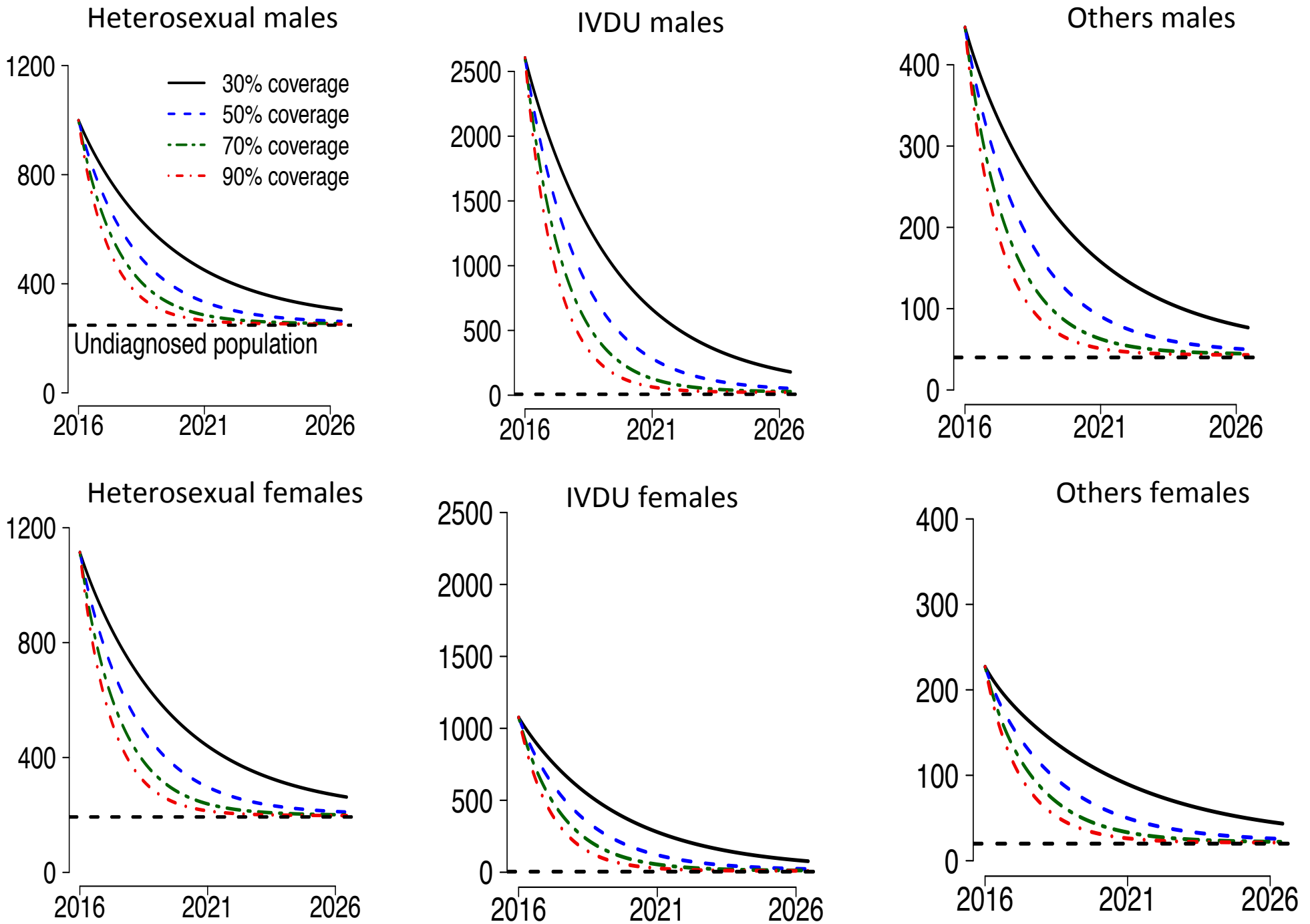
8 compartments dynamic model

+ undiagnosed population*

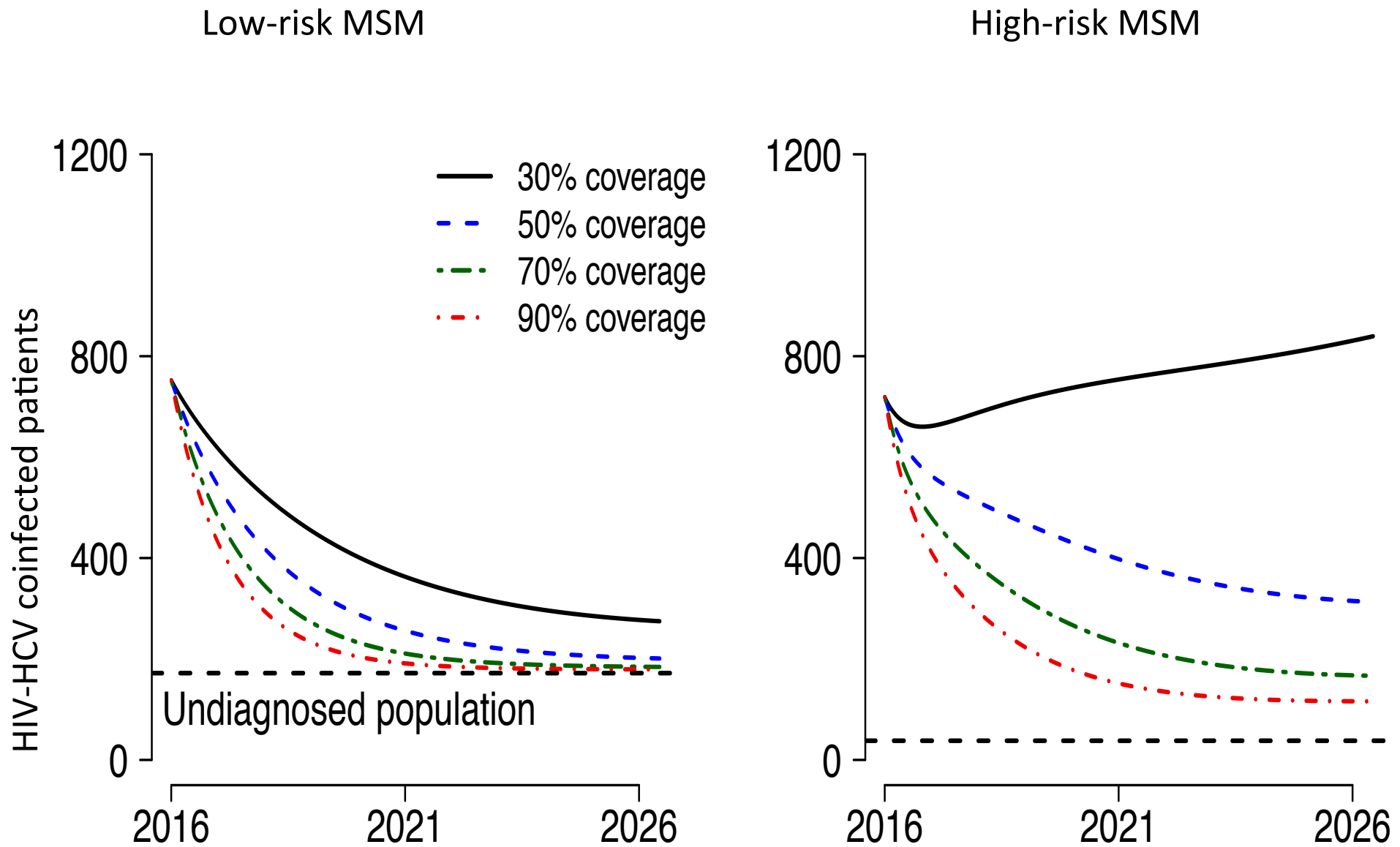
Projected HCV prevalence in the overall population



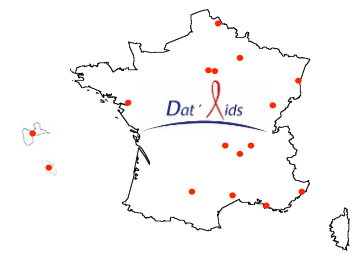
Projected HCV prevalence in different risk group



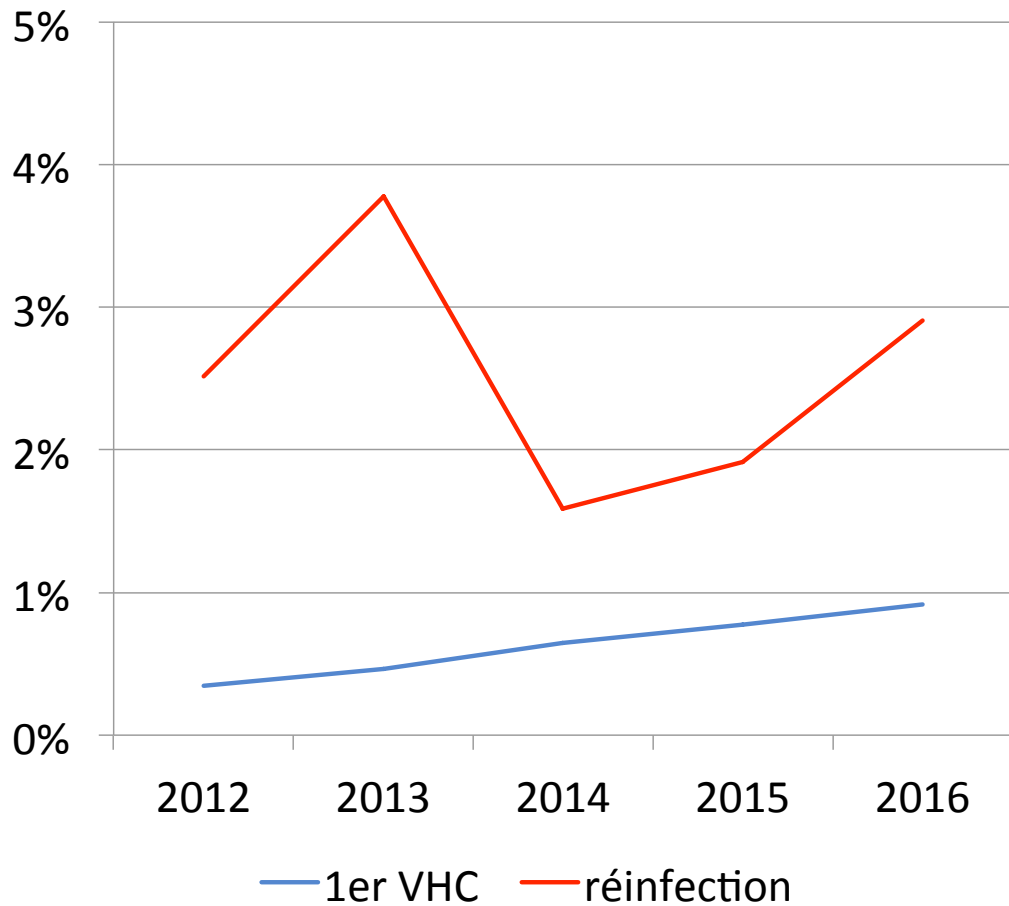
Projected HCV prevalence in MSM



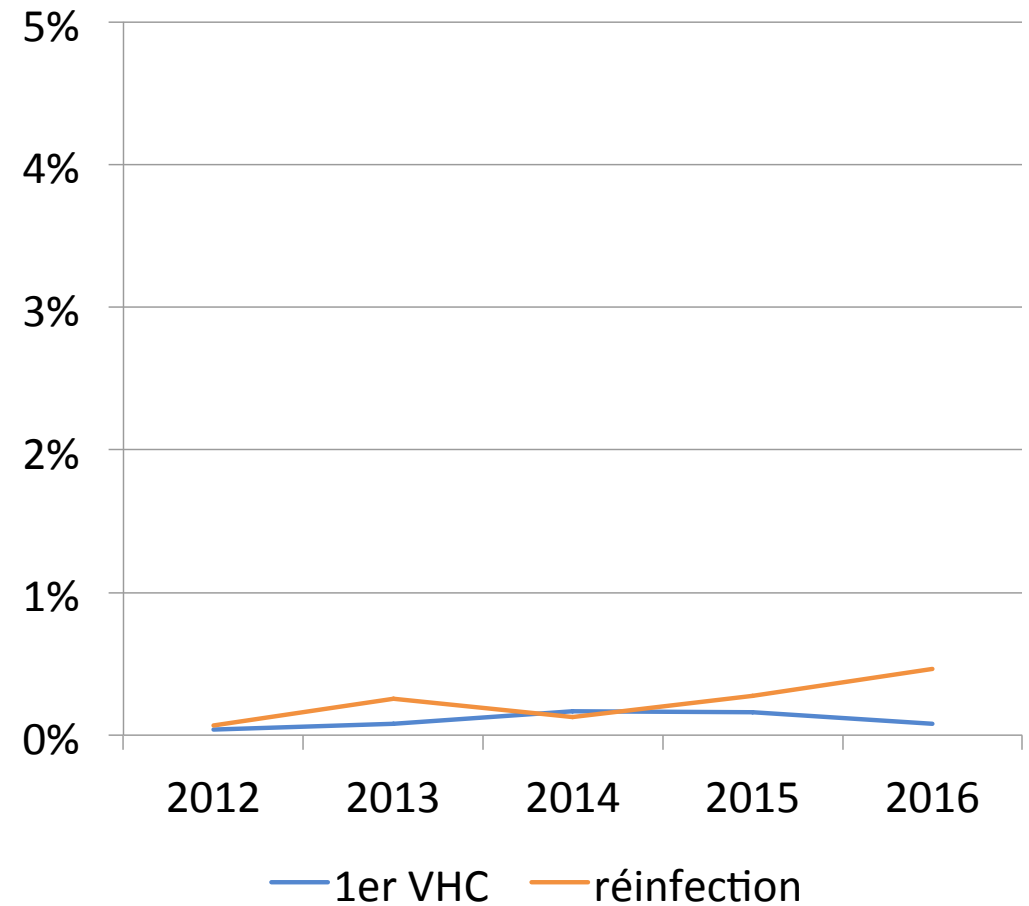
Incidence du VHC aiguë dans la cohorte DatAIDS



HSH



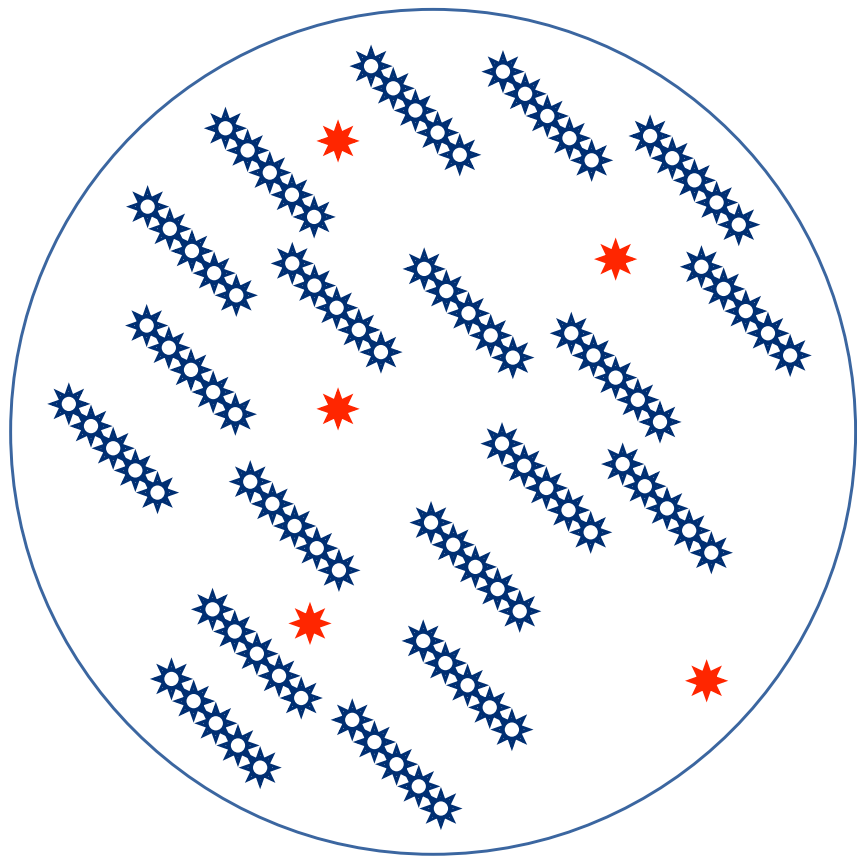
Autres



Determining Risk Markers for Gonorrhea and Chlamydial Infection and Reinfection Among Adolescents in Public High Schools

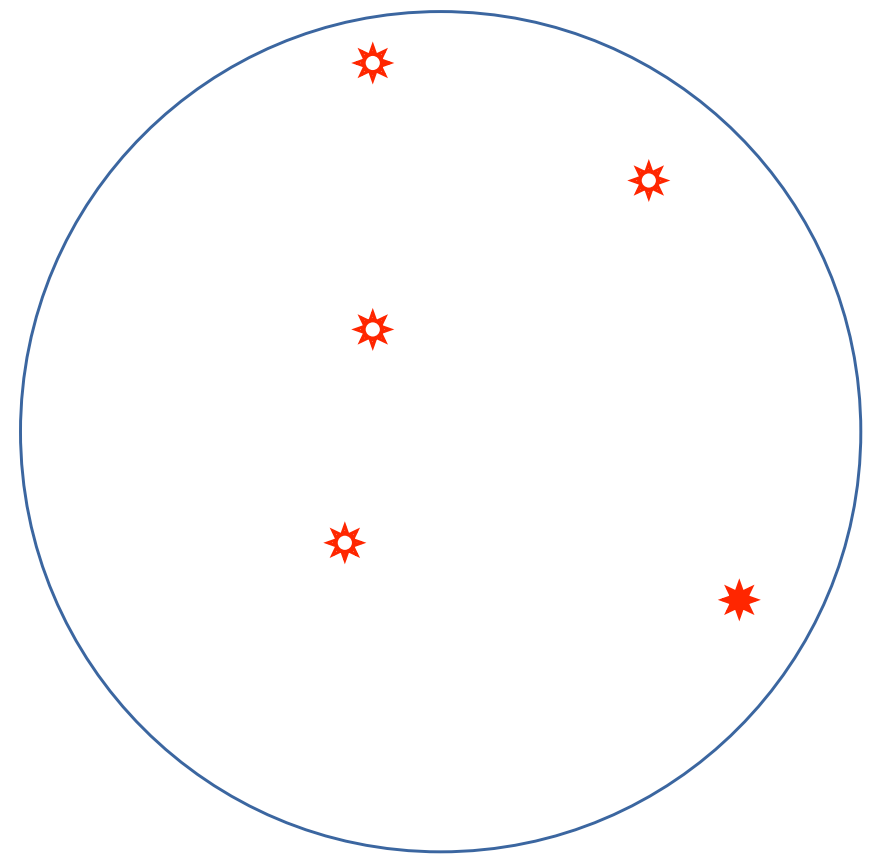
GRETA L. ANSCHUETZ, MPH,* JENNIFER N. BECK, MPH,*† LENORE ASBEL, MD,*‡ MARTIN GOLDBERG,*
MELINDA E. SALMON,*§ AND C. VICTOR SPAIN, DVM, PhD,*

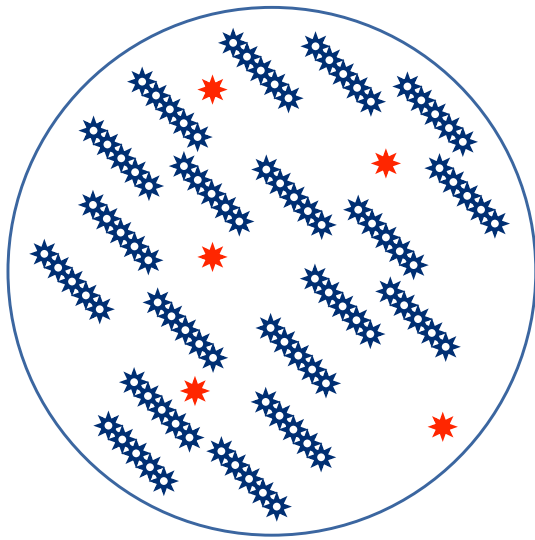
	♂	♀
Prévalence (%)	2.4	6.0
Incidence 1 ^{ère} infection (/100 PA)	2.2	5.5
Incidence réinfection (/ 100 PA)		
Partenaire identifié non traité	45.2	85.5
Autre situation	40.8	40.1



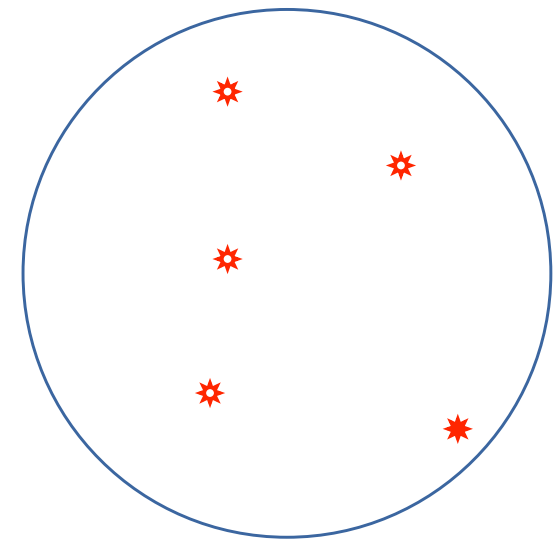
Incidence 1^{ère} infection

Incidence réinfection

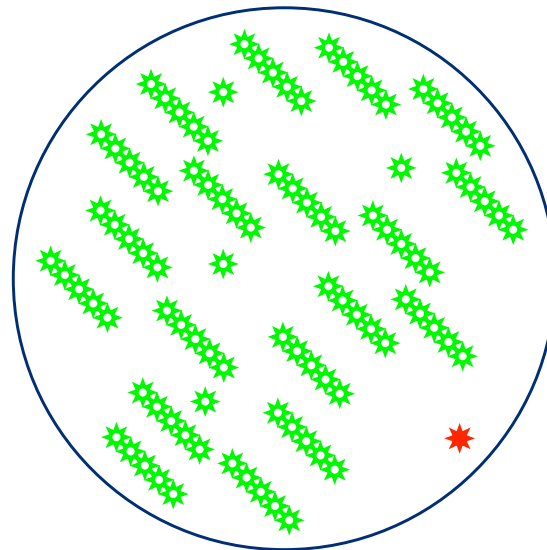




Incidence 1^{ère} infection MSM



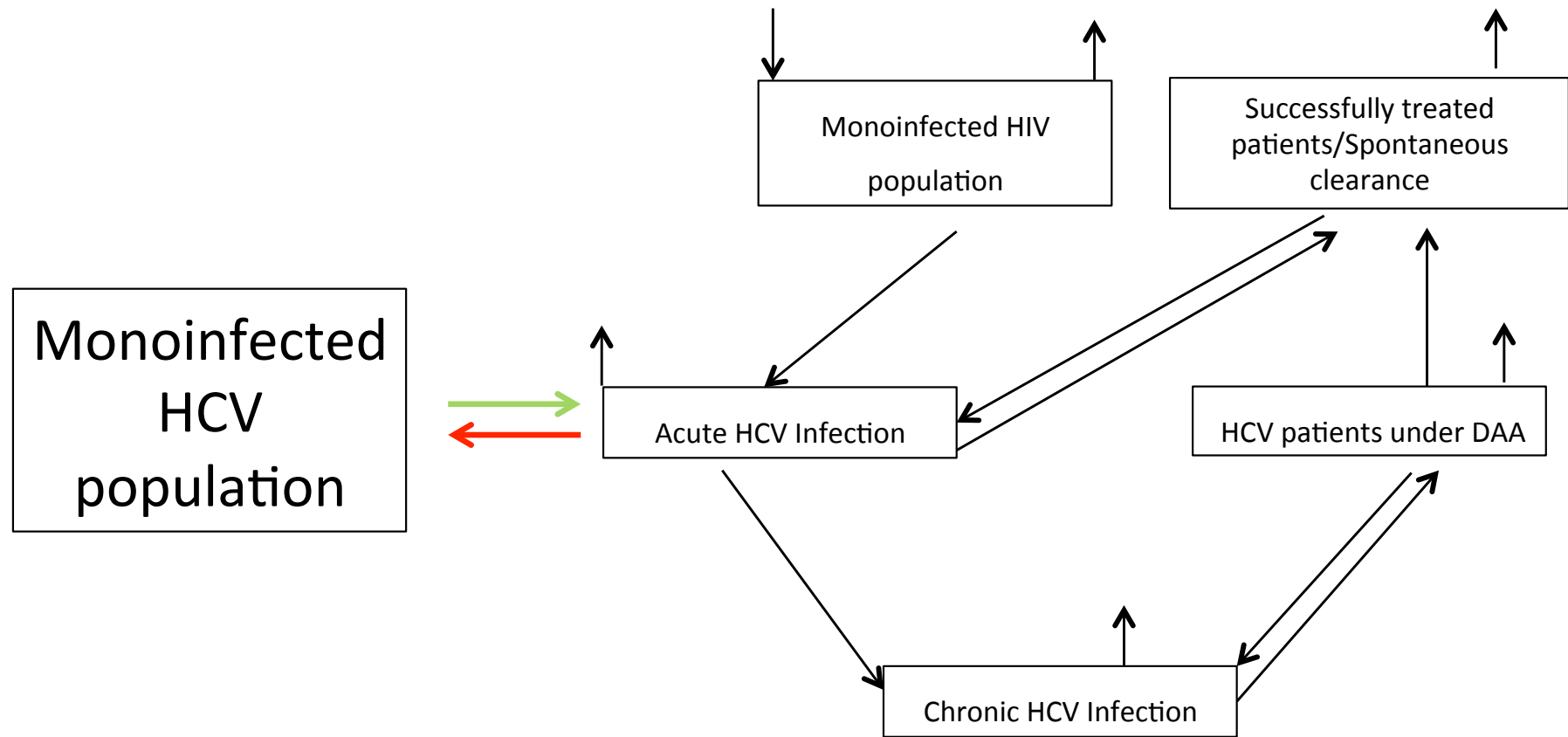
Incidence réinfection MSM
= incidence HR MSM



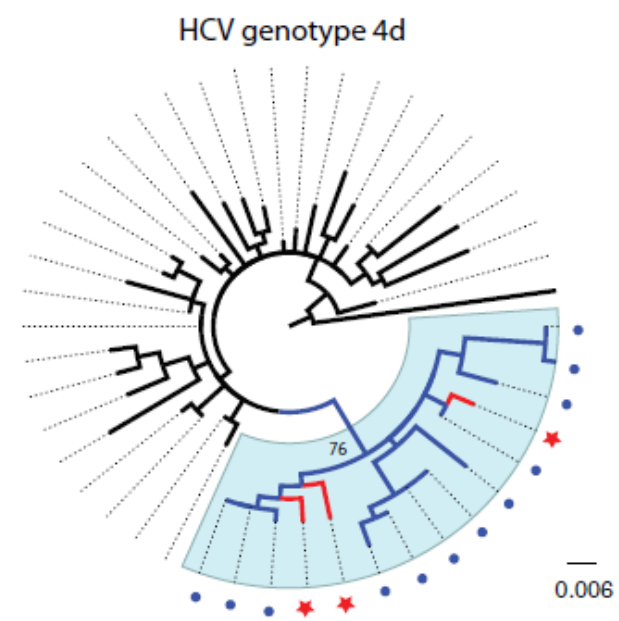
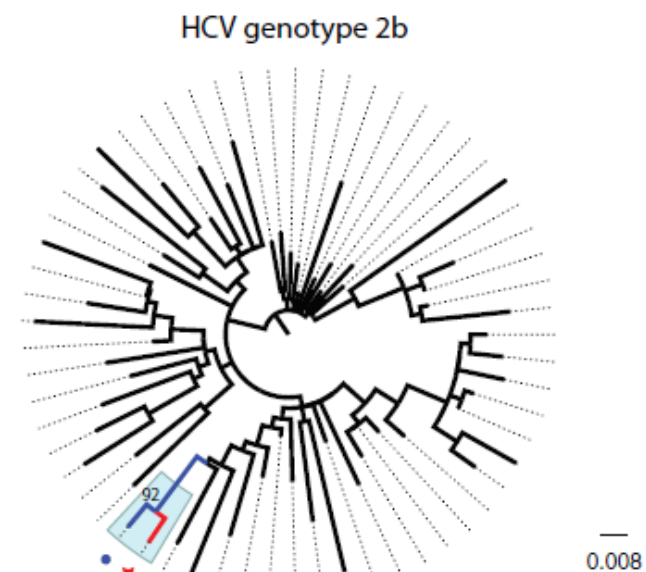
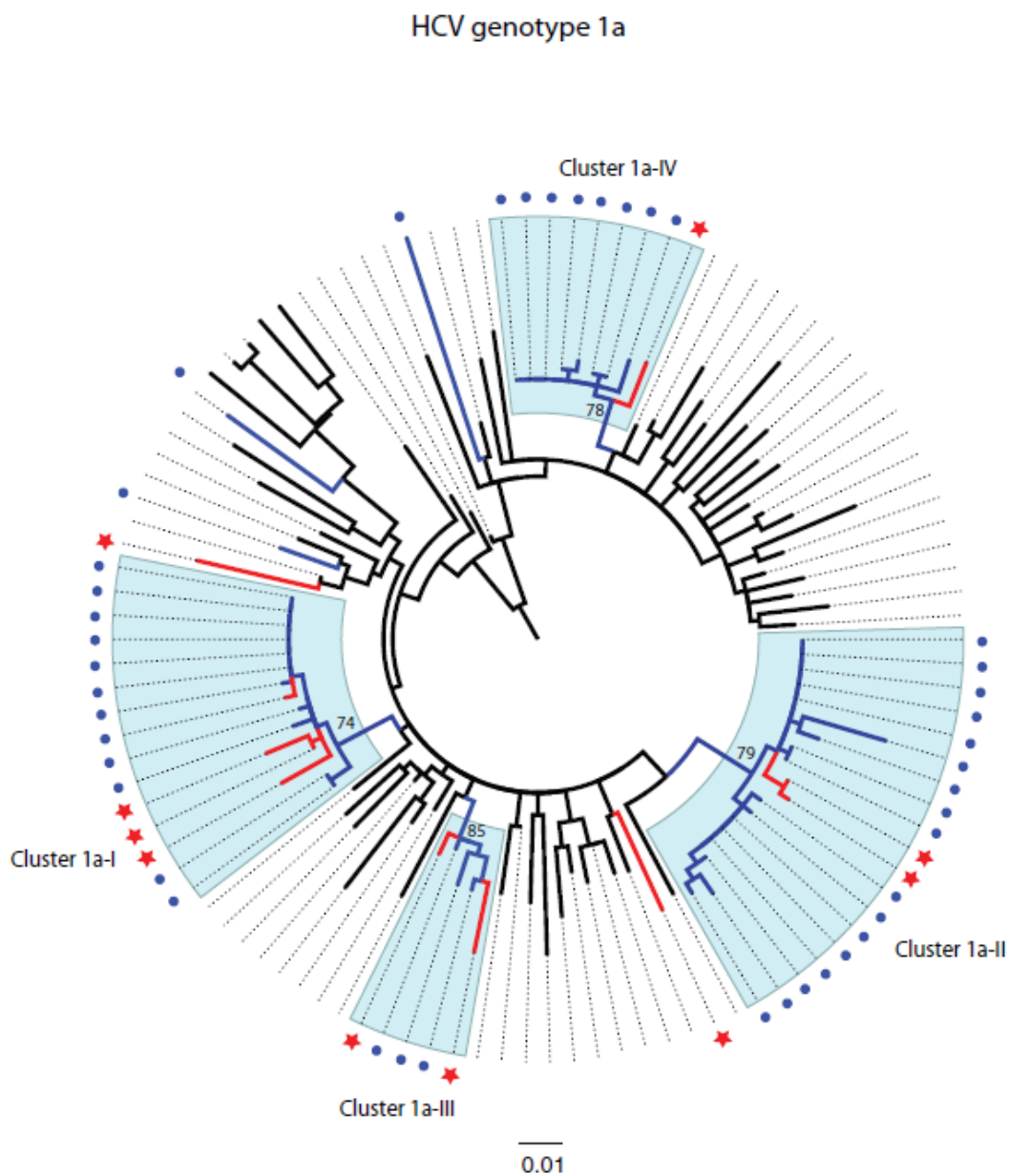
Incidence 1^{ère} infection autres patients
= incidence LR MSM

$$\% \text{ HR MSM} / \text{total MSM} = \frac{\text{incidence}_{\text{tous MSM}} - \text{incidence}_{\text{LR MSM}}}{\text{incidence}_{\text{HR MSM}} - \text{incidence}_{\text{LR MSM}}} = 18\%$$

Circulation du VHC entre HSH VIH+ et VIH- ?



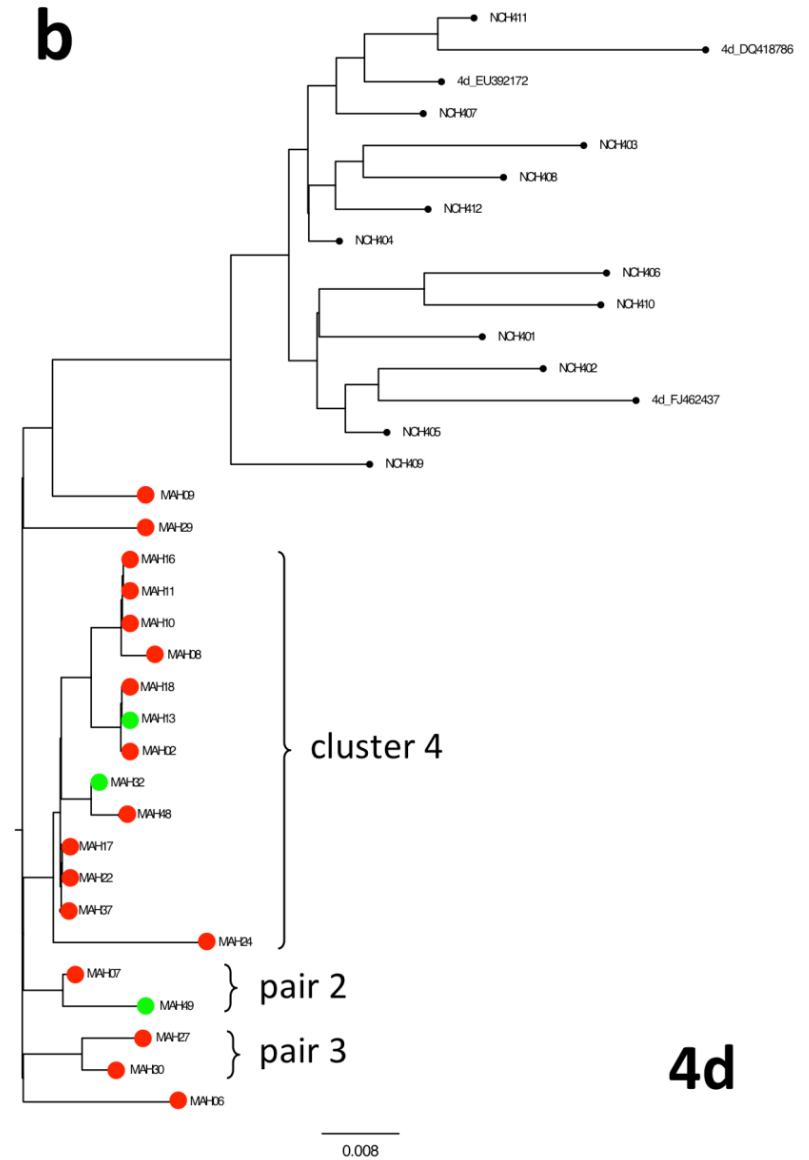
Clusters VHC chez HSH : Amsterdam cohort



Clusters VHC chez HSH VIH+ et VIH- à Lyon



Hospices Civils de Lyon

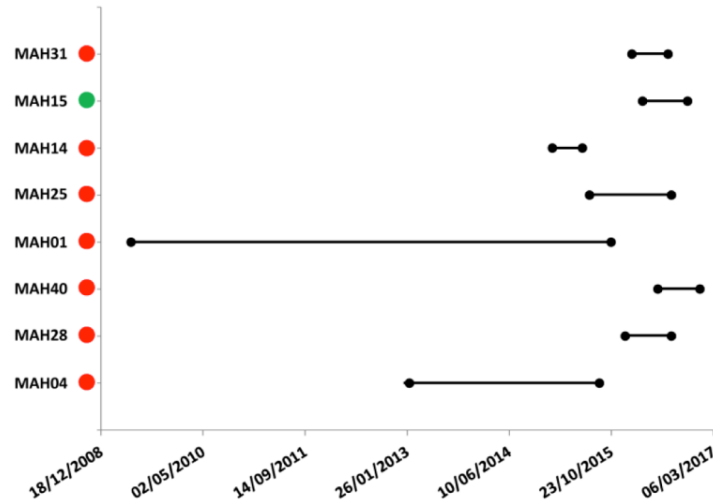


Chronologie d'infection dans 4 clusters

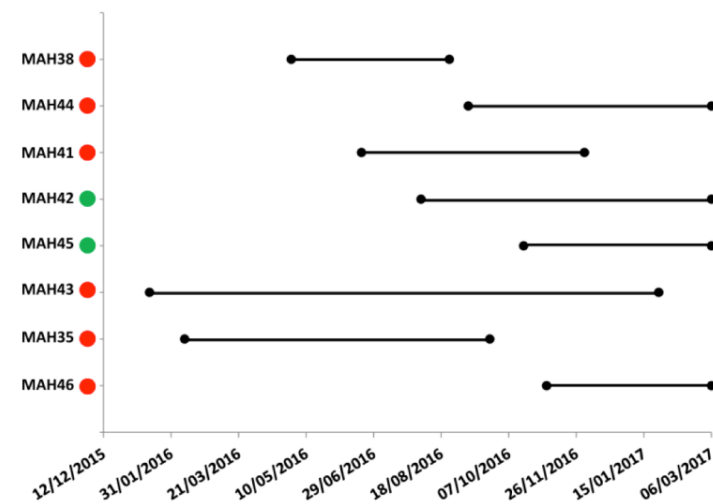


Hospices Civils de Lyon

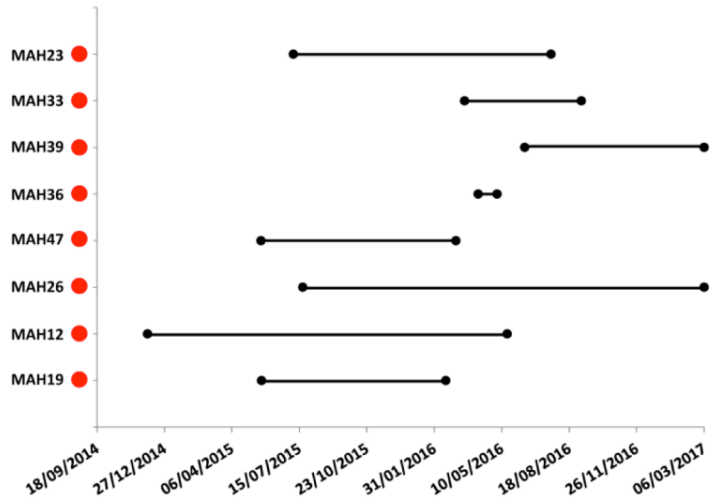
cluster 1



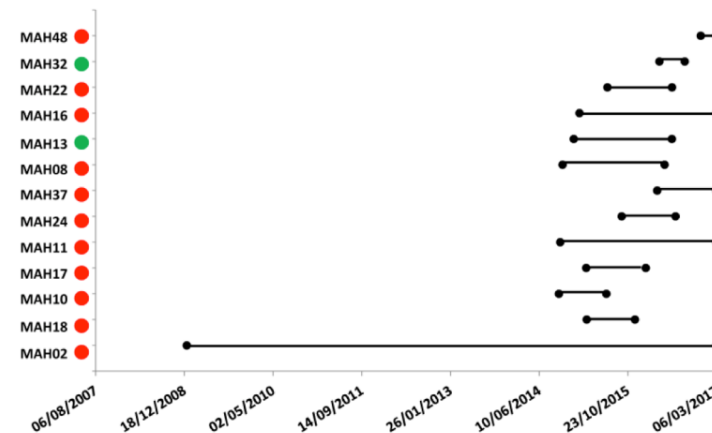
cluster 2



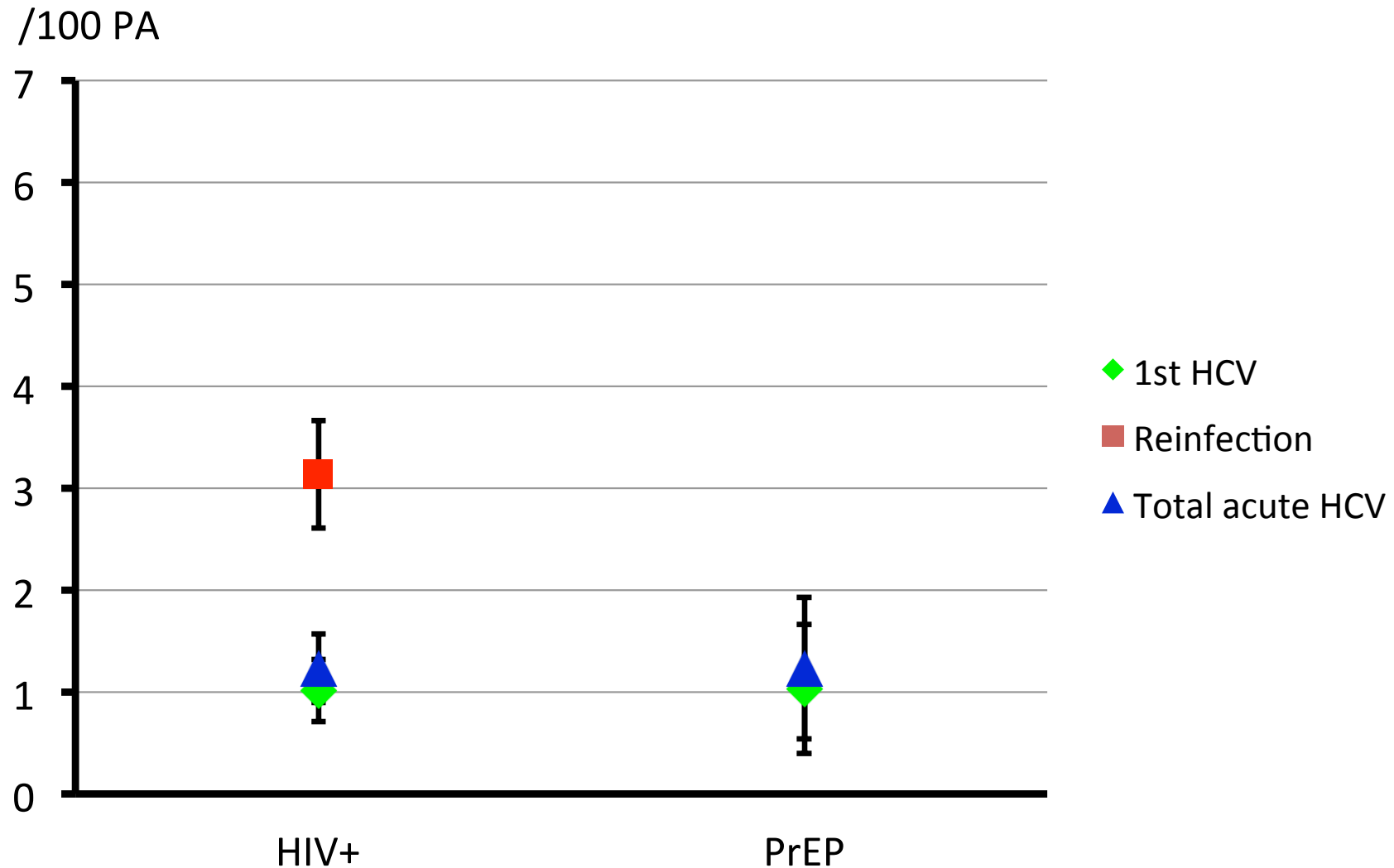
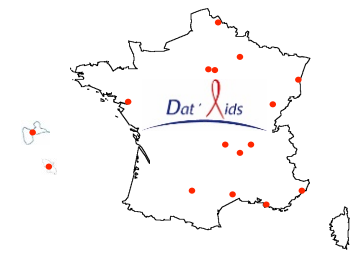
cluster 3



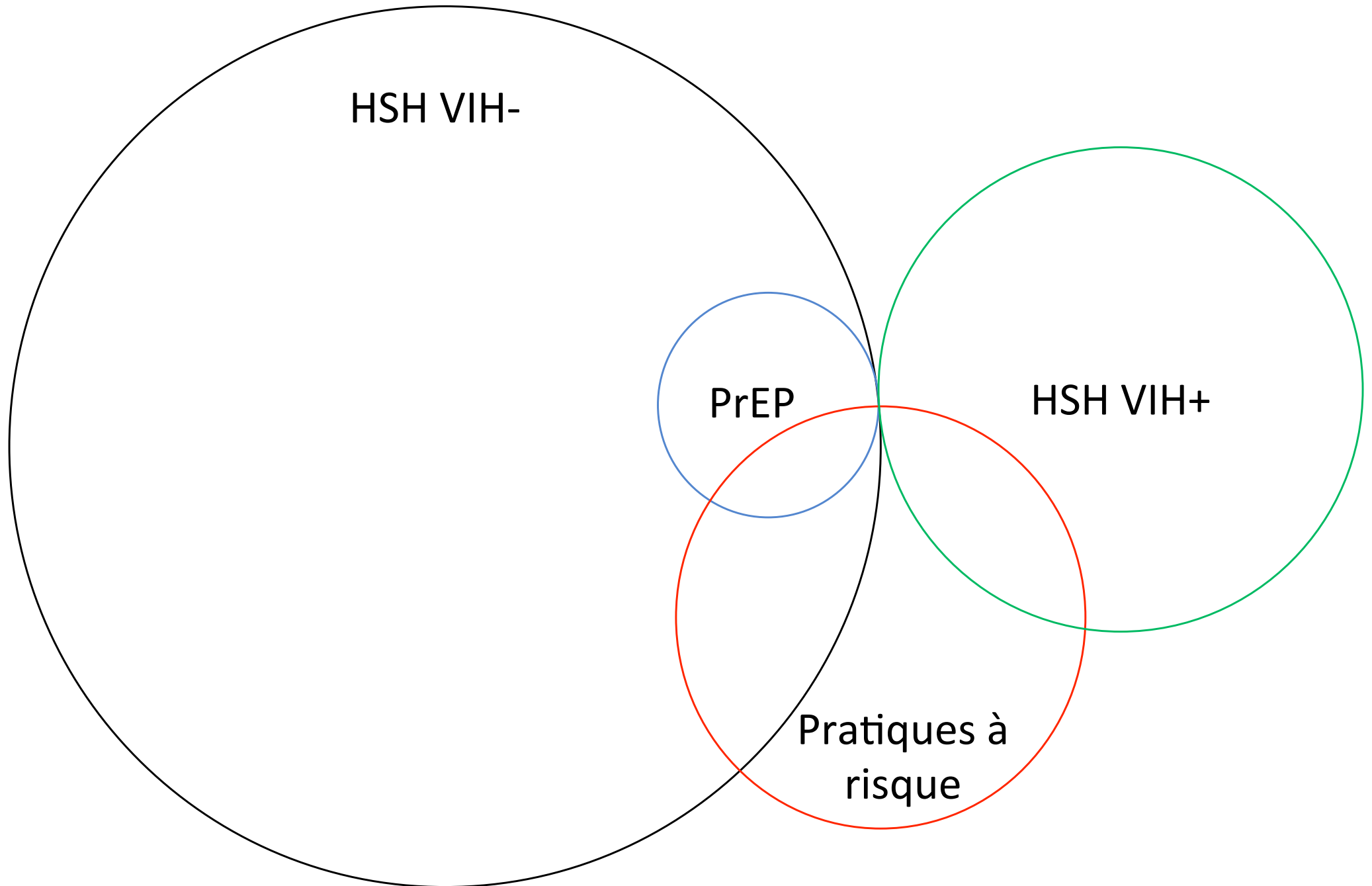
cluster 4



Incidence du VHC aiguë chez les HSH VIH+ et sous PrEP dans la cohorte DatAIDS



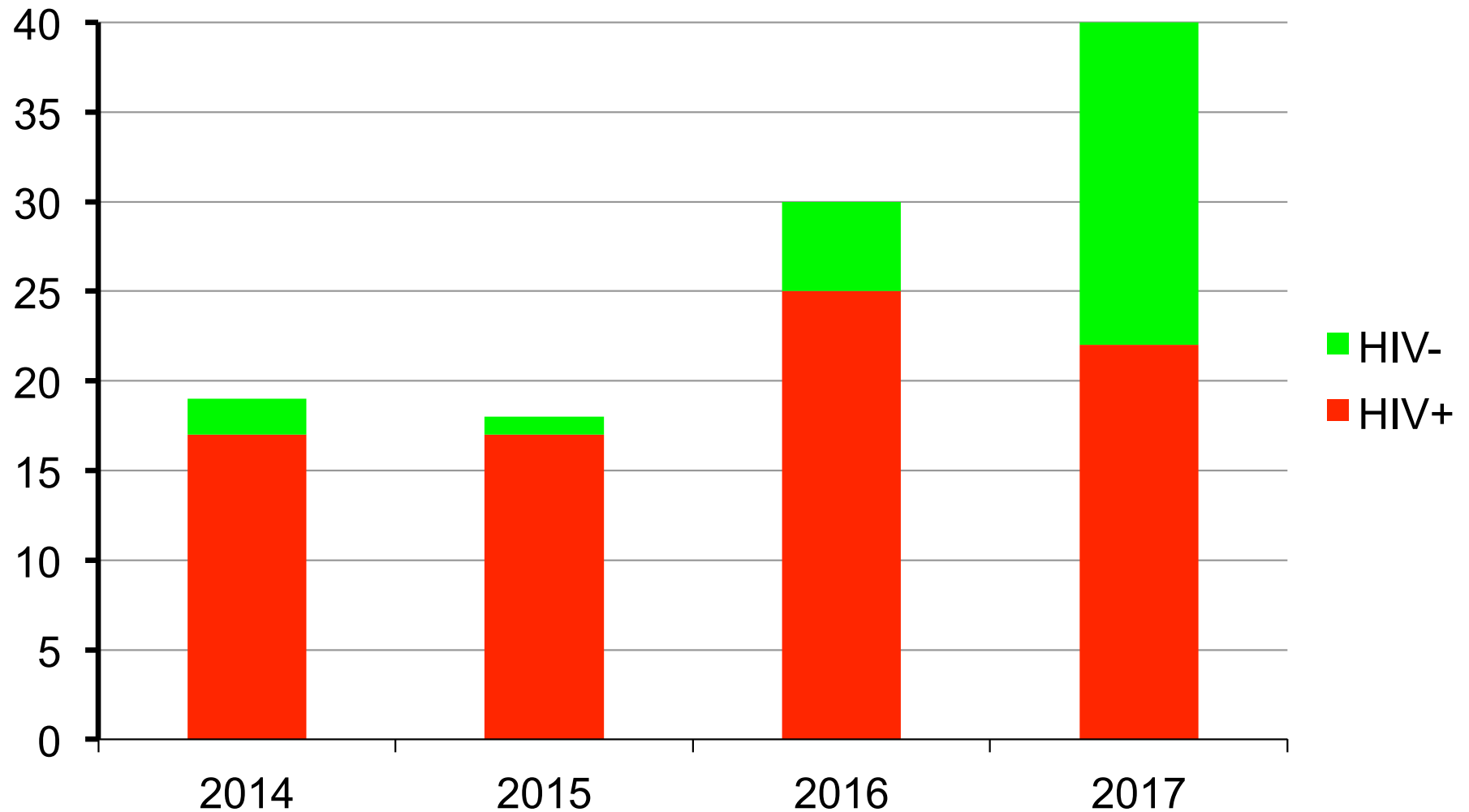
Circulation du VHC chez les HSH



Hépatites C aiguës chez les HSH Lyon, 2014-2017

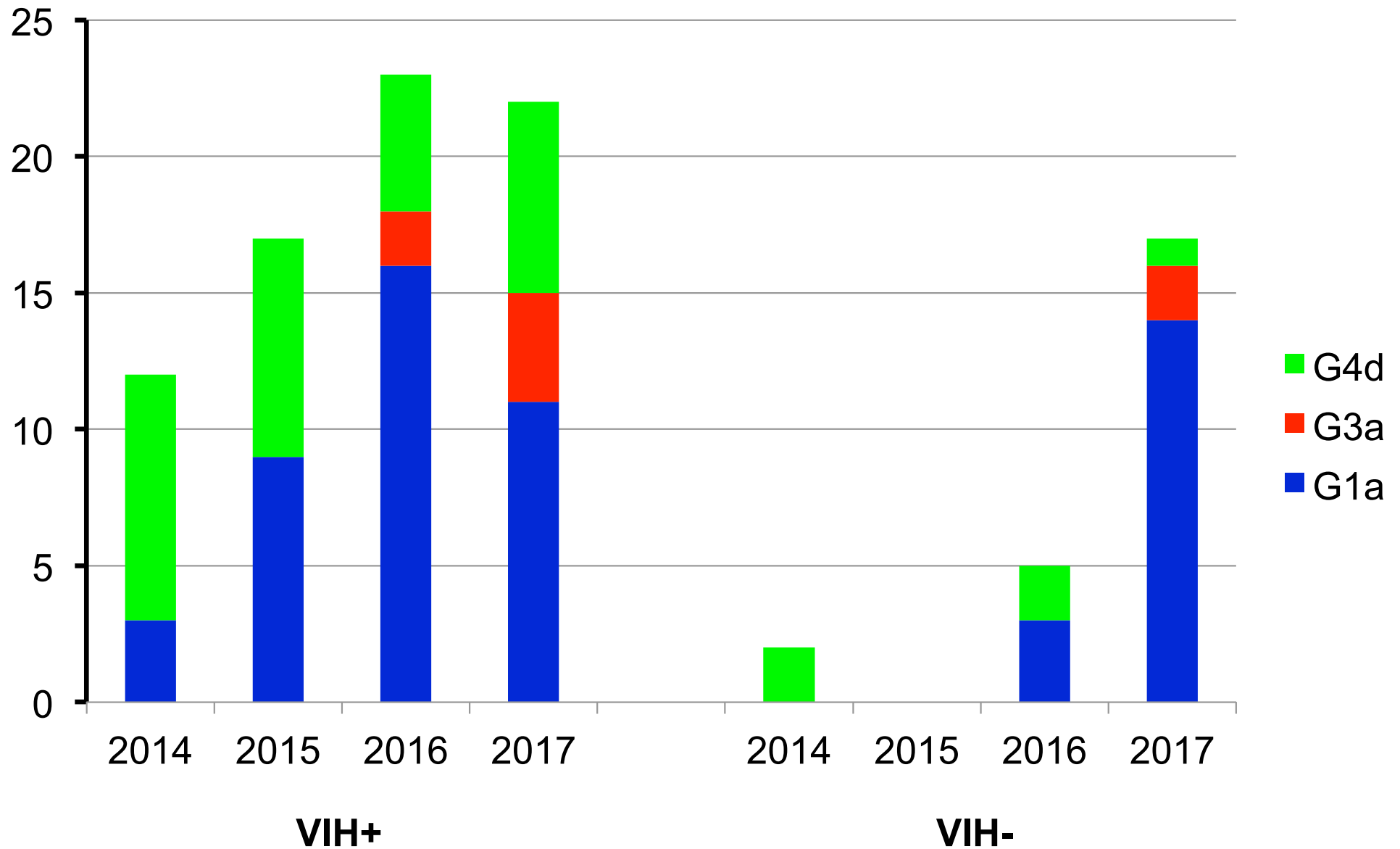


Hospices Civils de Lyon



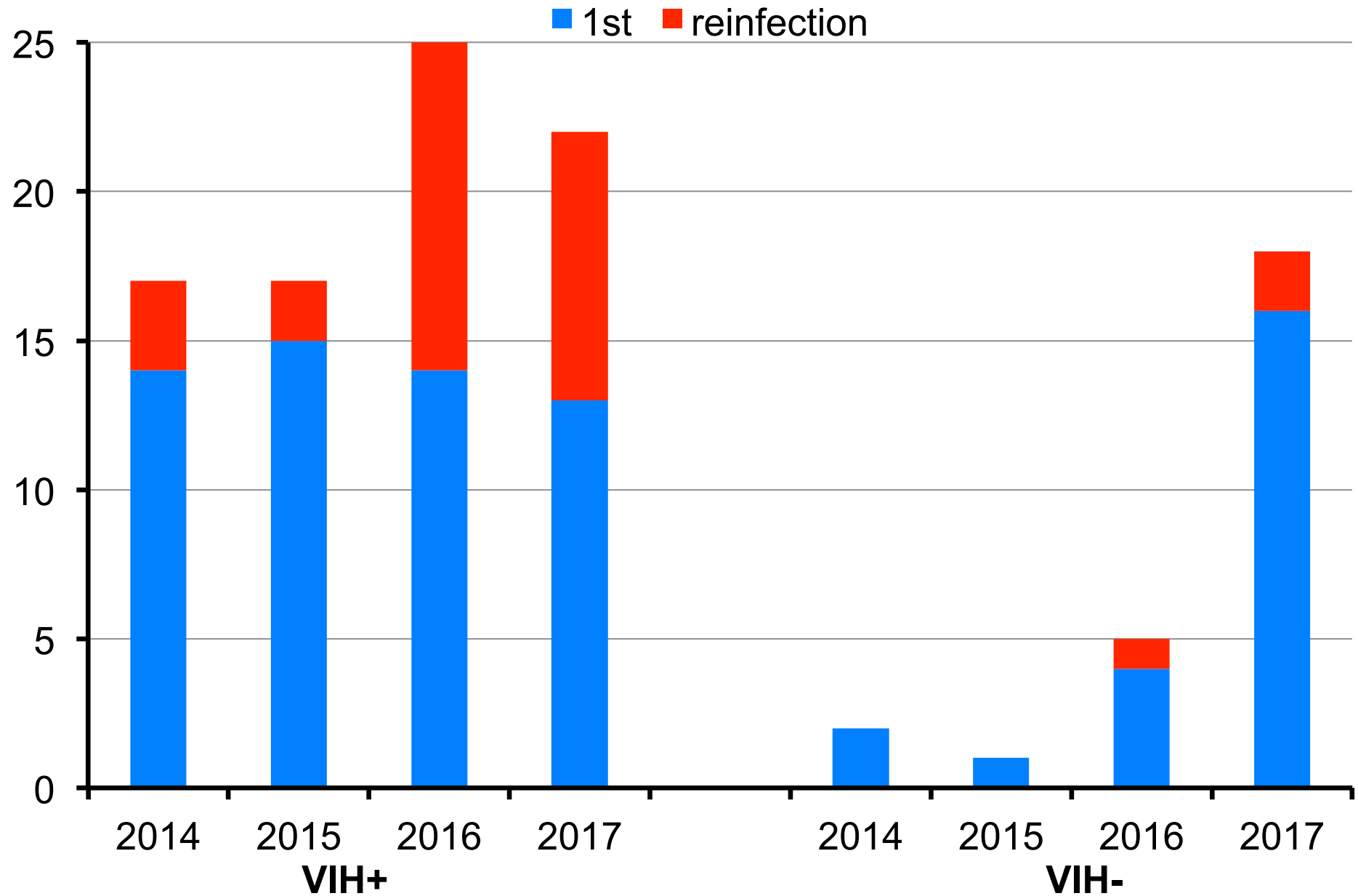


Evolution des génotypes / hépatites C aiguës





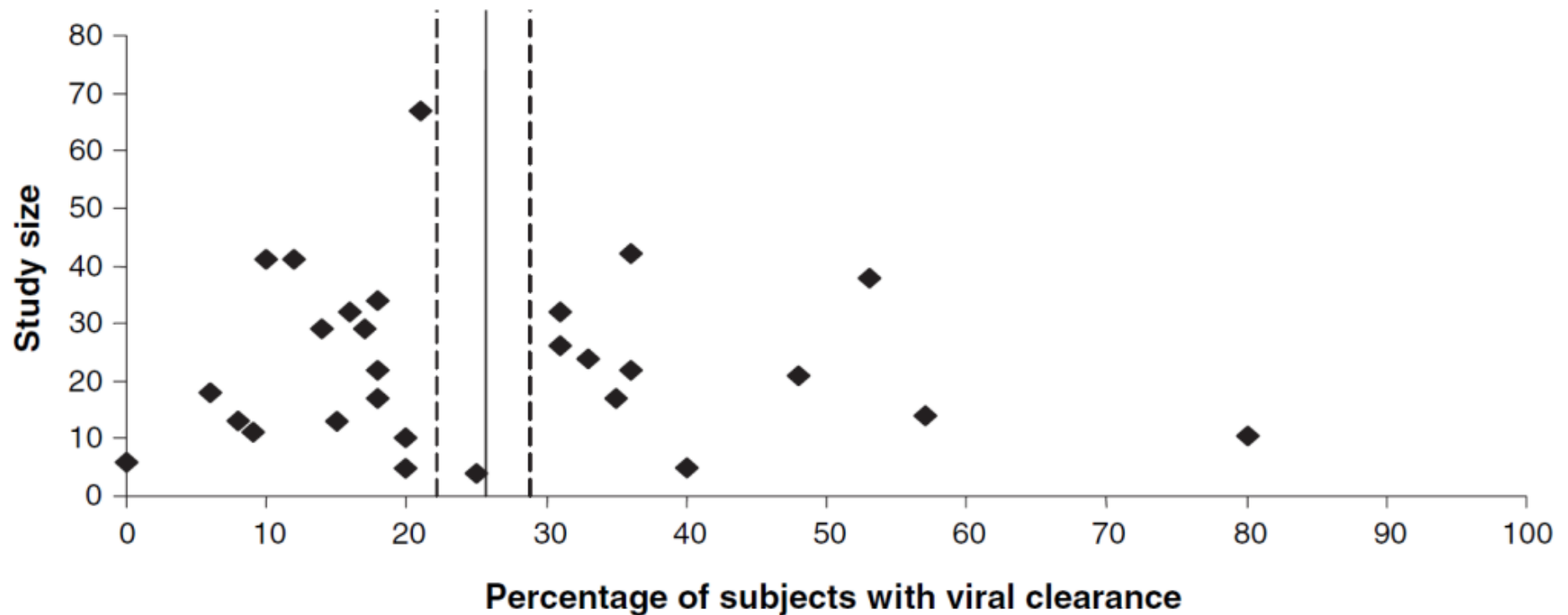
Réinfections / hépatites C aiguës



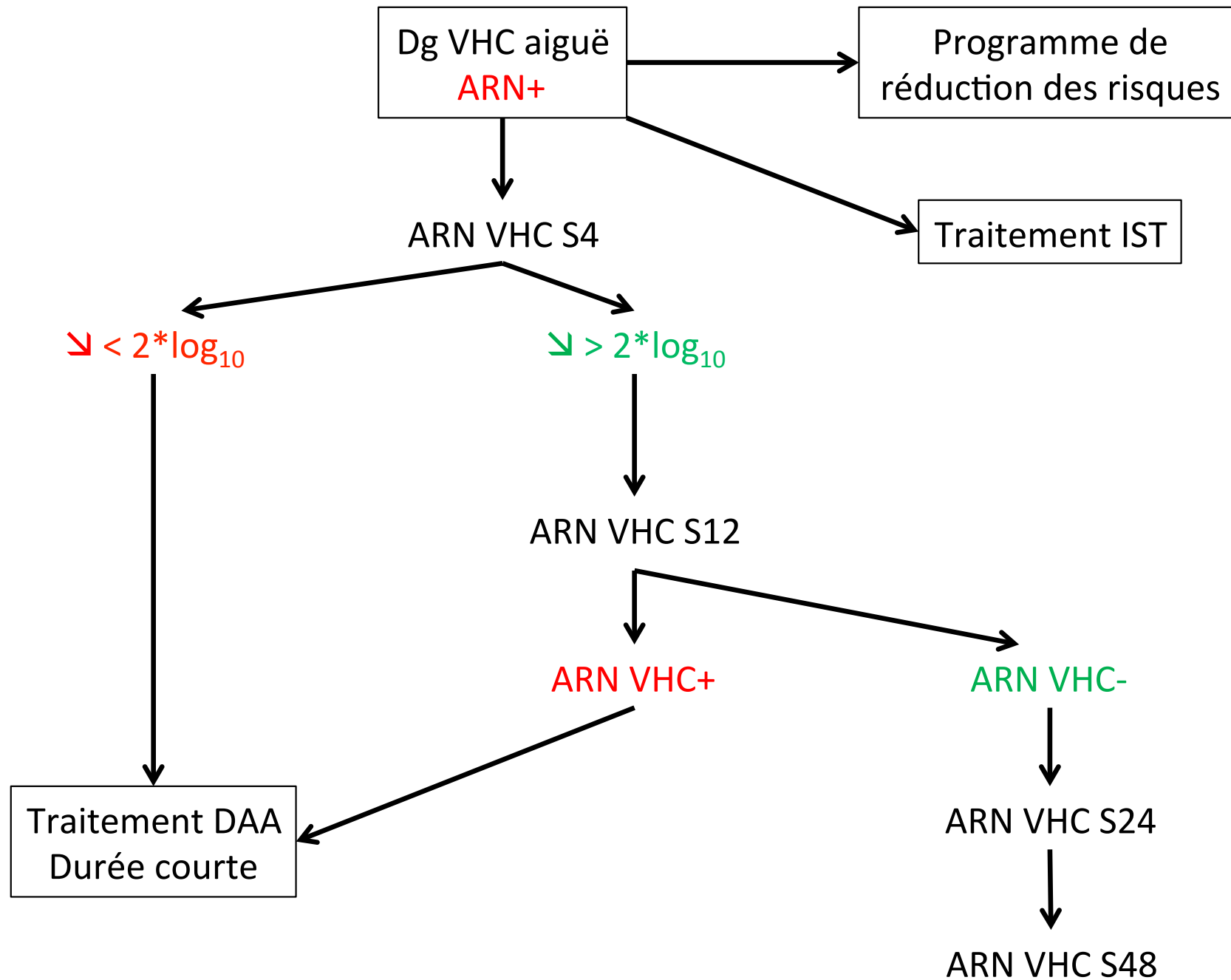
Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies

J. M. Micallef, J. M. Kaldor and G. J. Dore *National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Darlinghurst, Sydney, NSW, Australia*

★ Lyon 2014-2017 : 10%



Recommandations de prise en charge des hépatites C aiguës



RECOMMANDATIONS AFEF POUR L'ÉLIMINATION DE L'INFECTION PAR LE VIRUS DE L'HÉPATITE C EN FRANCE

- Traitement **sans délai**
- Mêmes schémas thérapeutiques qu'à la phase chronique
- Education thérapeutique

Conclusions (1)

- Les rechutes VHC tardives (post-RVS) sont rares, les réinfections fréquentes
- La réinfection VHC est fréquente si les pratiques à risque persistent (IVDU, HSH HR)
- Le nombre de réinfection ↗ avec le taux de traitement (et de guérison)
- Le ratio (incidence réinfection / incidence 1^{ère} infection) est fonction de la proportion de patients HR : plus ce ratio est élevé, moins la population à risque est importante
- Le taux de guérison spontanée des hépatites C aiguës chez les HSH est de l'ordre de 10%; ce taux ne diffère pas entre 1^{ère} hépatite et réinfection
- Le taux de RVS est comparable entre 1^{ère} infection et réinfection
- L'hépatite C aiguë chez les HSH est une IST, quel que soit son mode de transmission

Conclusions (2)

- L'élimination du VHC chez les patients coïnfectés par le VIH ne sera possible que si l'on contrôle également l'épidémie VHC chez les HSH HR
- Le VHC circule depuis plusieurs années des HSH VIH+ → HSH VIH-
- Le suivi PrEP permet d'identifier les hépatites C aiguës dans cette population
- Le contrôle de l'épidémie chez les HSH nécessitera:
 - Un dépistage régulier du VHC chez les HSH VIH+ et VIH-
 - Un dépistage régulier des recontaminations chez les patients guéris
 - Un suivi des génotypes à l'échelle individuelle (réinfections) et à l'échelle de la population (épidémiologie)
 - Le traitement précoce de toute infection aiguë, 1^{ère} infection ou réinfection
 - Des mesures de réduction des risques ciblées

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