Insights into Hepatitis C Virus Infection Studies of Infected Donors and Recipients

Prevalence, incidence and molecular characteristics in blood donors

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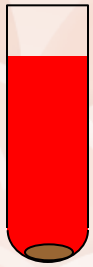
Blood Systems

HCV is etiological agent of NANB

Choo, Kuo, Weiner, Overby, Bradley & Houghton

Science (1989) 244:359-362



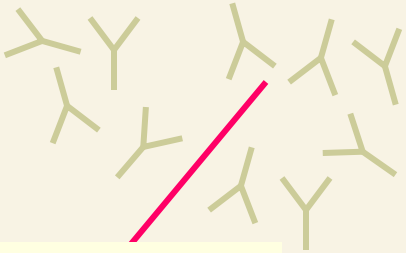
Ultracentrifuge
NANBH-Infectious
Chimpanzee Plasma

Pellet

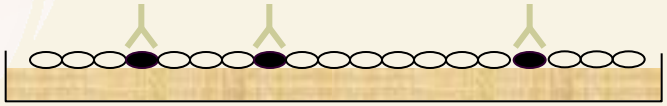
Extract total
RNA+DNA

Serum Antibodies

PT-NANBH
Patients



Incubate



Bacterial cDNA libraries in "expression" vector λgt11

DETERMINE PROPERTIES OF CLONE 5-1-1

- *Extra*-chromosomal
- Derived from RNA (~9600 nt) found *only* in NANBH samples
- Encodes protein that binds antibodies found *only* in NANBH infections

IDENTIFICATION OF HEPATITIS C VIRUS (HCV)

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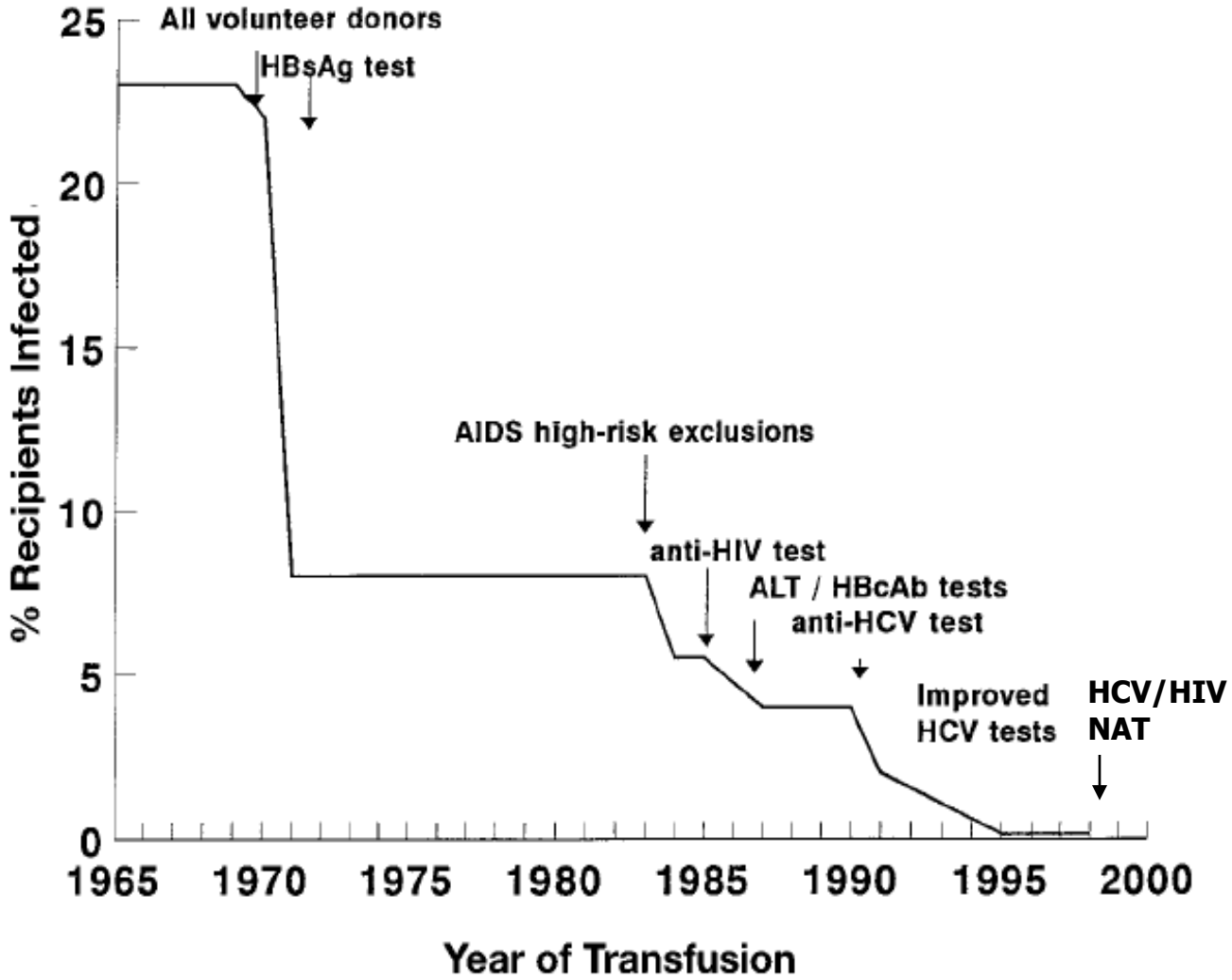
Declining Risk of HCV from Blood Transfusions



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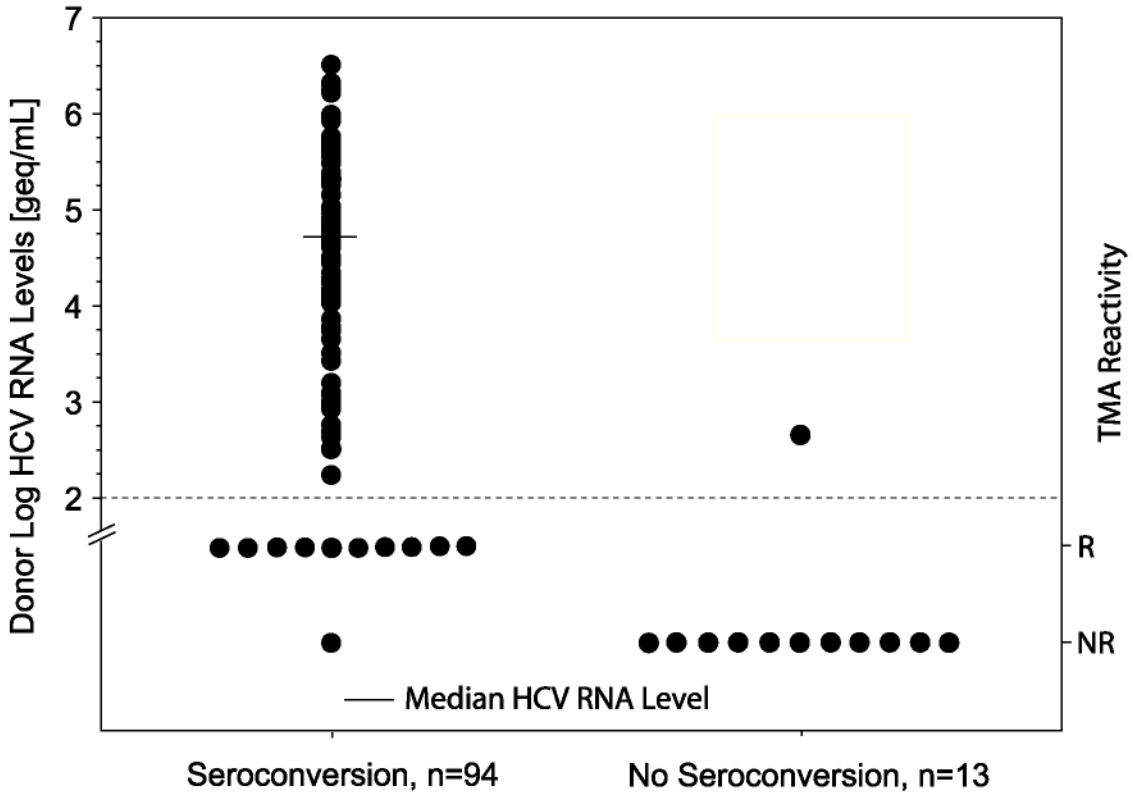
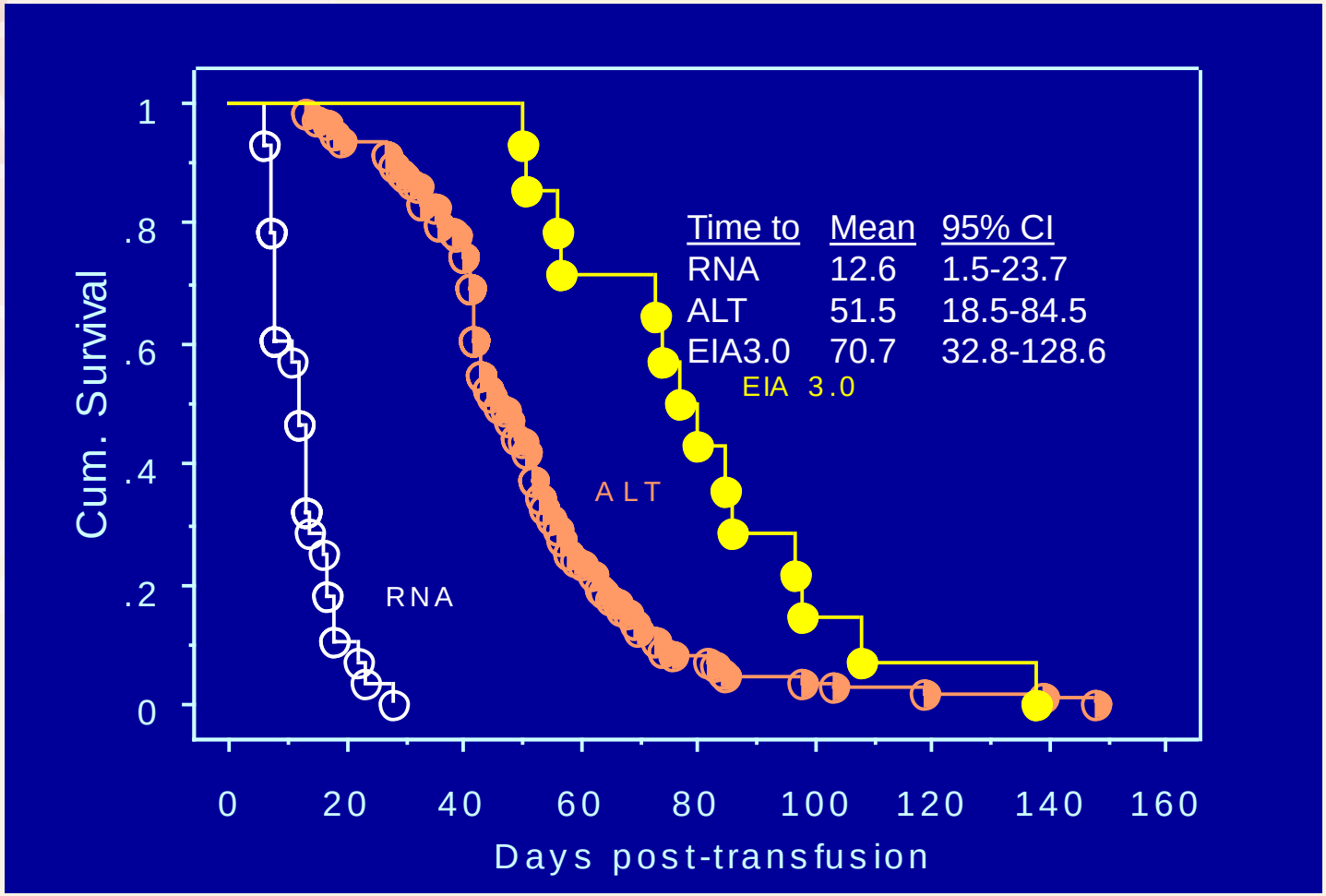
Viral load distribution in 117 HCV seropositive TTVS donors relative to transmission to recipients



Blood Systems

Operskalski, Mosley, Busch, Transfusion , 2003

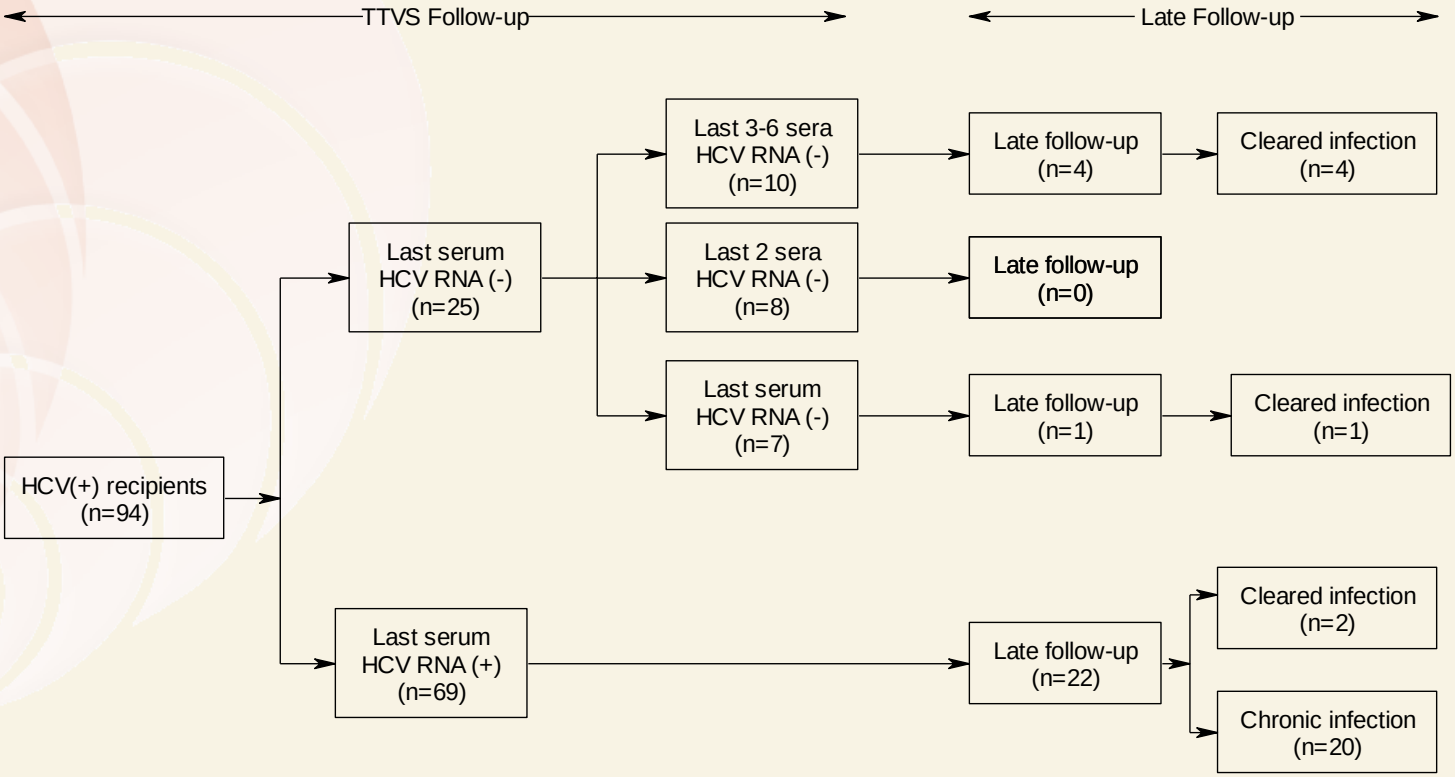
Time to detection of HCV markers among 94 infected recipients in TTVS



Blood Systems

Busch et al, Transfusion, 2006

Clearance of acute HCV based on TMA of stored serum from the TTVS and NHLBI long-term f/u study



27 % early resolution, median 21 weeks after ALT elevation (5-43 weeks)
8 % of early "carriers" resolved 2-10 years later (Seeff et al.)
Resolution more common in women (3-fold) and symptomatic (2-fold) cases
No correlation with age, genotype or early profiles of viremia/ALT elevation
Intercalated negative RNA (TMA) results peri-SC not predictive of clearance

Blood Systems

Mosley et al., Hepatology, 2005; Gastroenterology, 2008

Blood and Source Plasma Collections in U.S.

Whole Blood & RBC/Platelet Apheresis

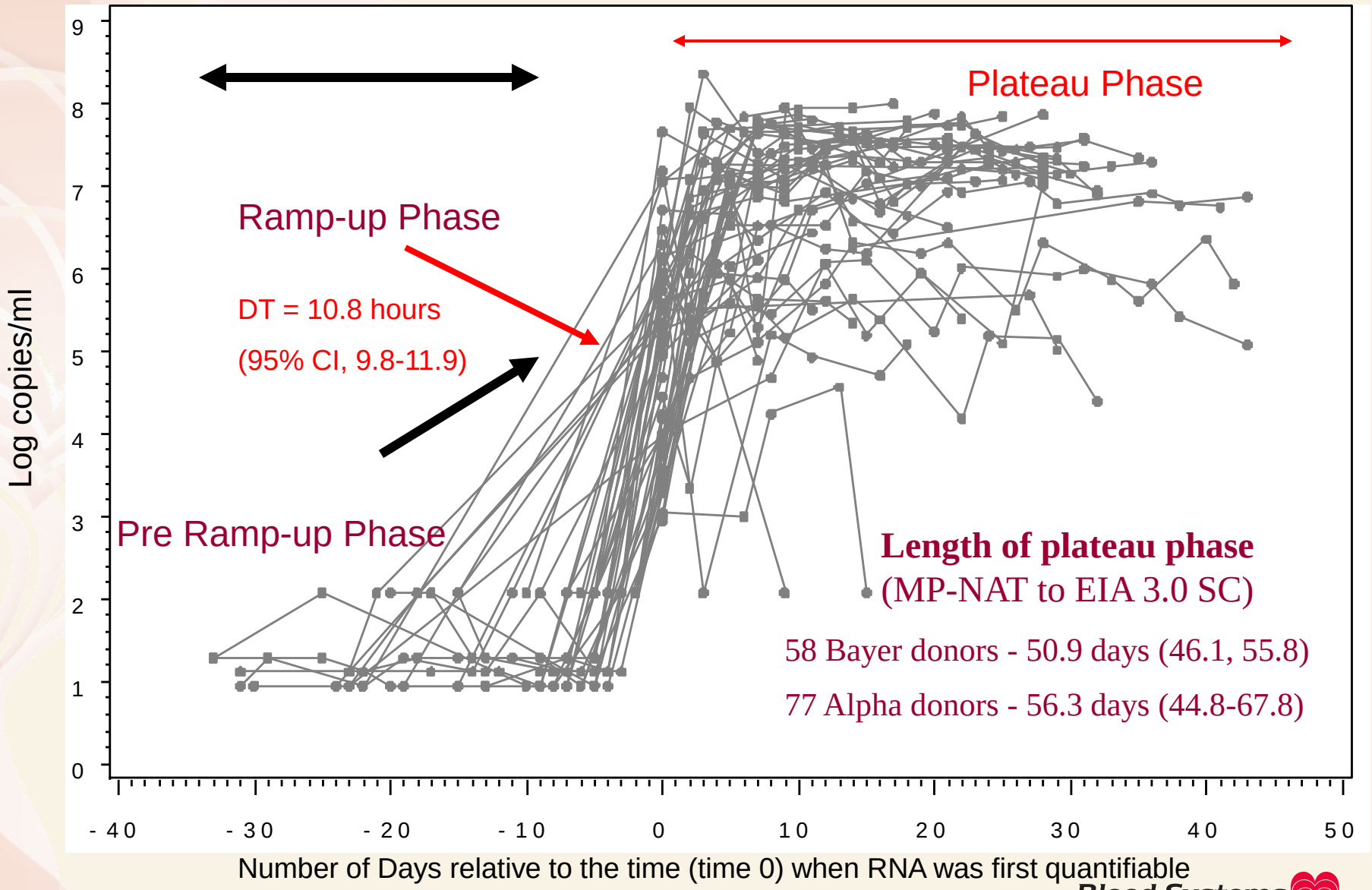
- 17 million donations annually from ~9 million donors
- ~10 large networks (ARC, BSI, etc) plus 50 indep blood centers
- 500 mL WB yield pRBC and 200 ml plasma components
- 90% apheresis platelets
- 80% repeat (1.7x/yr);20% FT donors
- No financial reimbursent
- Components transfused directly to ~13 million recipients

Source Plasma Collection

- 13 million U.S. collections from 750,000 donors annually
- 400 collection centers
- 17 donations/year
- 500 – 880 mls plasma /collection
- Paid $25-$50 /donation
- Pooled, fractionated, inactivated

Blood Systems

Viral Load in Early Hepatitis C Virus Infection, 55 plasma donors



Blood Systems

Glynn et al. Transfusion, 45:994-1002, 2005

STUDY DESIGN

Experiment I (Infectivity of very early ramp-up plasma)

Plasma pheresis donors

Serial infusions of 50 mL/donor

HCV Naive Chimp X355

Serial F/U for HCV Infection

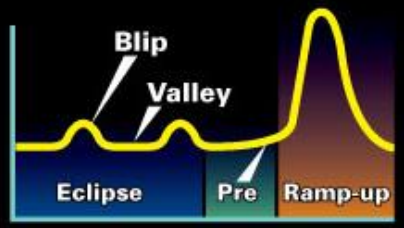
Identification of Infectious Donor by Sequencing

Determining infectivity of earlier samples from the implicated donor

HCV Naive Chimp X331

Serial F/U for HCV Infection

Experiment II (Infectivity of eclipse phase plasma)



Serial donor samples

Phase 1 250 ml pool of valley phase

Phase 2 Sequential blip infusions 50 mL/donorX5

Phase 3 Pre and ramp-up infusions

Chimp X331

Serial F/U for HCV Infection

Experiment III (Rechallenge of transiently infected chimp)

Chimp X355
3 years after recovery

Challenge with 50 mL

containing 80 HCV RNA copies (1.6 cop/mL) from the previously infecting donation

serial follow-up for HCV infection

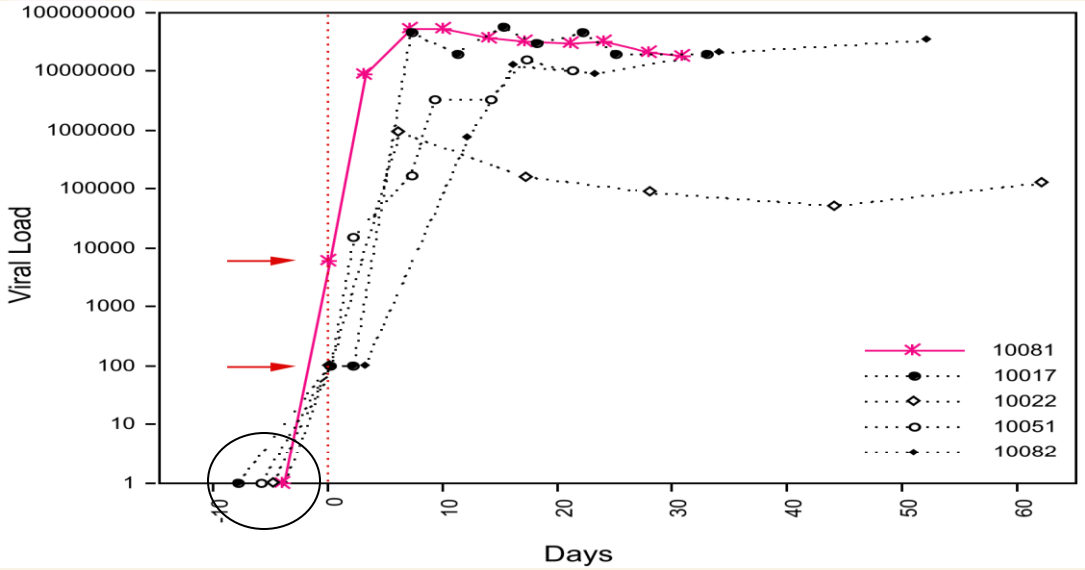
Rechallenge with 50 mL

containing 300,000 HCV RNA copies (6000 cop/mL) from the same donor

Serial F/U for HCV Infection

HCV transmission to a chimp from WP plasma from HCV infected plasma donors

- 50 ml plasma infused from each of five plasma donors who later tested HCV NAT+
- Transmission occurred and was molecularly linked to a single donor
  - plasma collected ~10 days prior to NAT detection
  - sample RNA+ on 2/24 HCV TMA assays (~1 gEq/6 mL)



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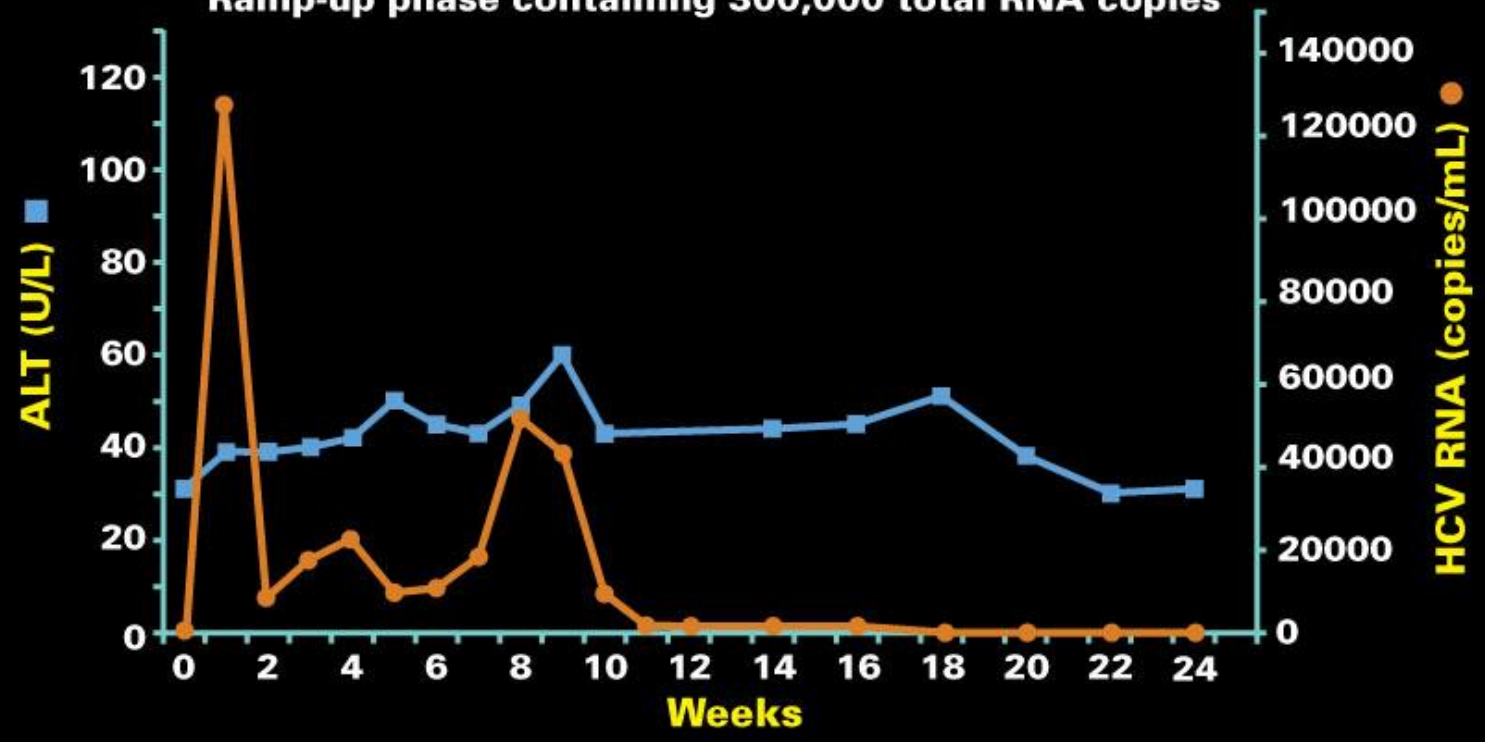
CHALLENGE STUDIES IN CHIMP X331

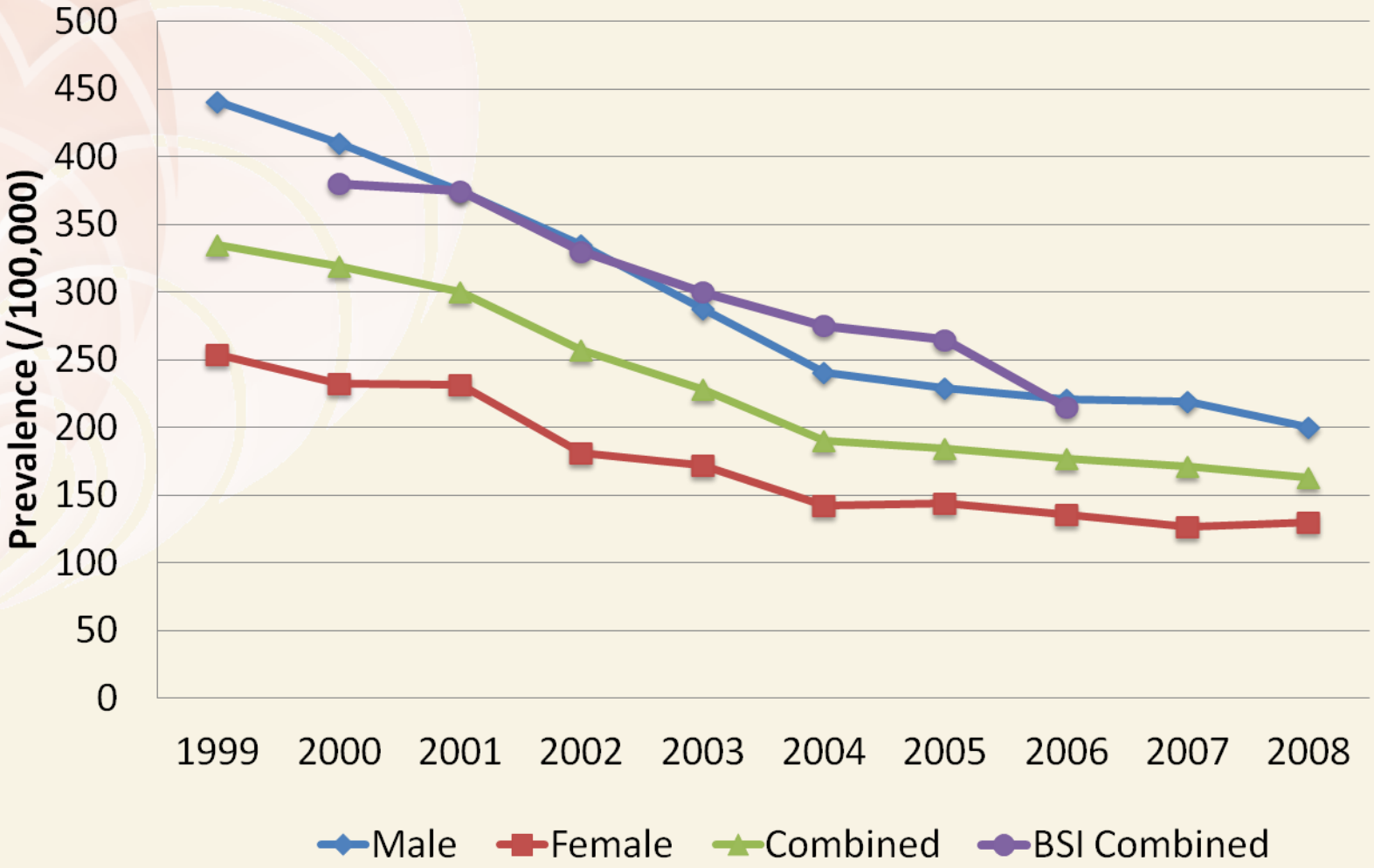
Valley Phase Infusions 50ml X 5	→	No Infection
Blip Phase Infusions 50ml X 5	→	No Infection
Pre Ramp-up (TMA+/PCR-) 50ml X 5	→	No Infection

ANTI-HCV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HCV-RNA	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-

Ramp-up phase containing 300,000 total RNA copies



HCV Prevalence in First Time Donors, ARC & BSI



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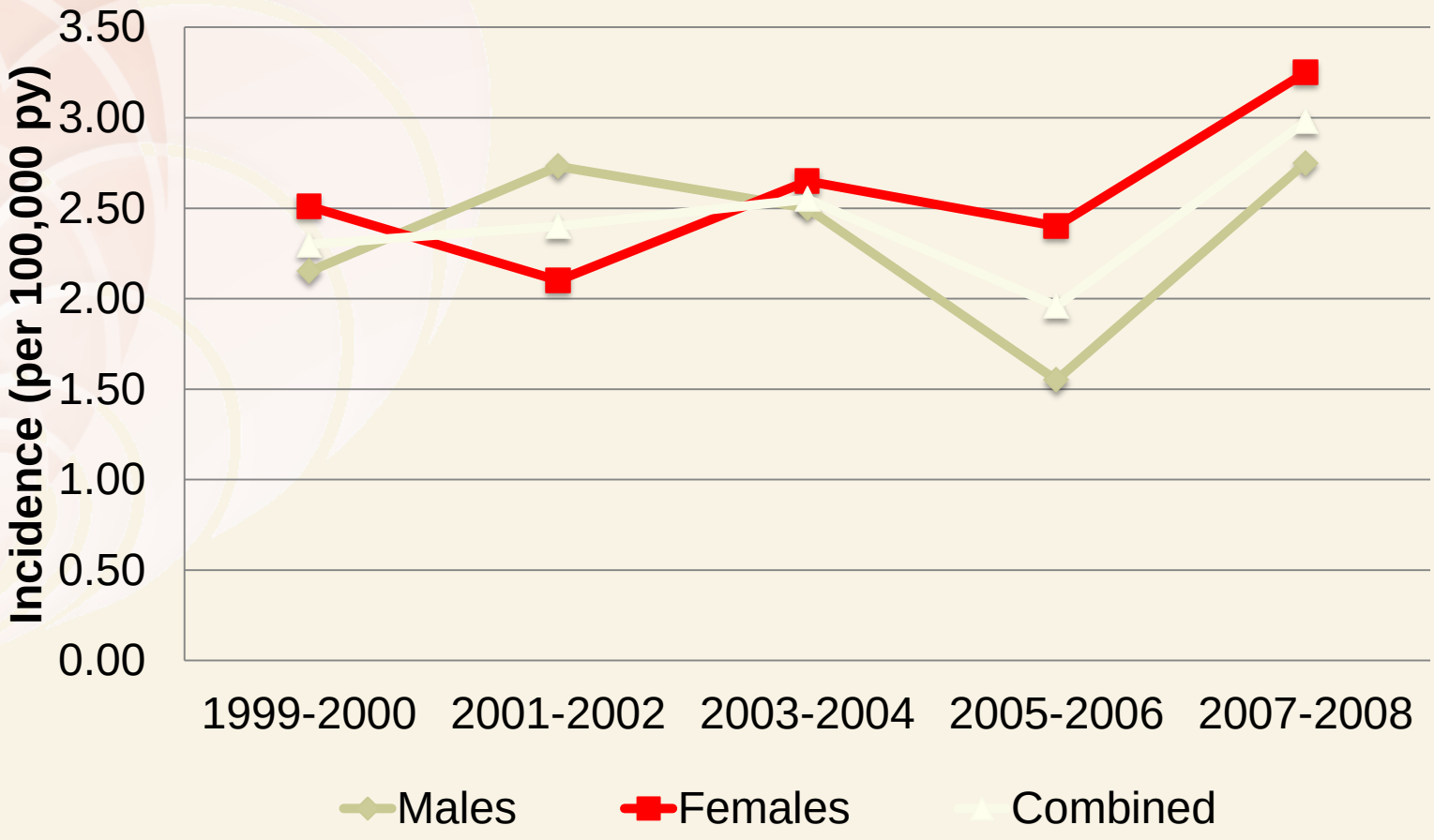
Zou S, Transfusion, 2010. Early Online

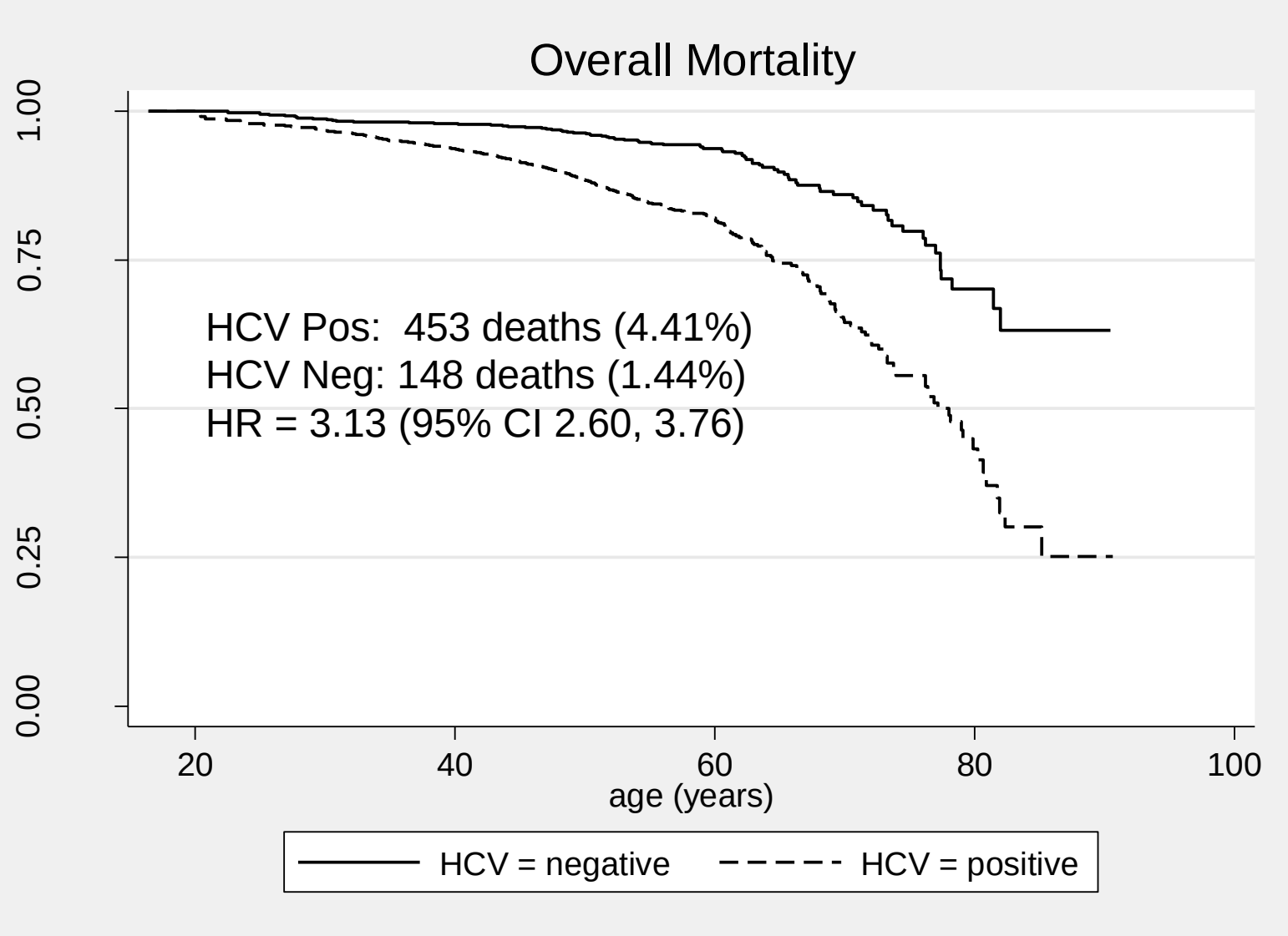
HCV Incidence in Repeat Donors



Zou S, Transfusion, 2010. Early Online

Retrospective Cohort Study of HCV Mortality in 10,000 HCV Ab+ and 10,000 Ab- Donors

Guiltinan Am J Epidemiol 2008



Cause of Death by HCV status

Cause of Death	HCV+ (N=10,259)	HCV- (N=10,259)
Cancer (excl Liver)	56	53
Cardiovascular	60	28
Trauma (Suicide)	106	36
Liver (& liver CA)	90	2
Drug/ETOH	64	6
Stroke	13	6
Infection	23	2
Other/Unknown	33	8
All Deaths	453	148

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HCV and Mortality

Cause of Death	HCV+	HCV-	HR (95% CI)
HCV	14	0	∞
“Other viral hepatitis”	13	0	∞
Liver disease	47	1	50.9 (7.0-368.6)
Liver cancer	16	1	16.6 (2.2-125.5)
All Liver deaths	90	2	46.0 (11.3-186.7)
Cancer (excl Liver)	56	53	1.1 (0.8-1.6)
Cardiovascular	60	28	2.2 (1.4-3.5)
Infection	23	2	11.7 (2.8-49.8)
Trauma/Suicide	106	36	3.0 (2.1-4.4)
Drug/ETOH	64	6	10.8 (4.7-25.0)

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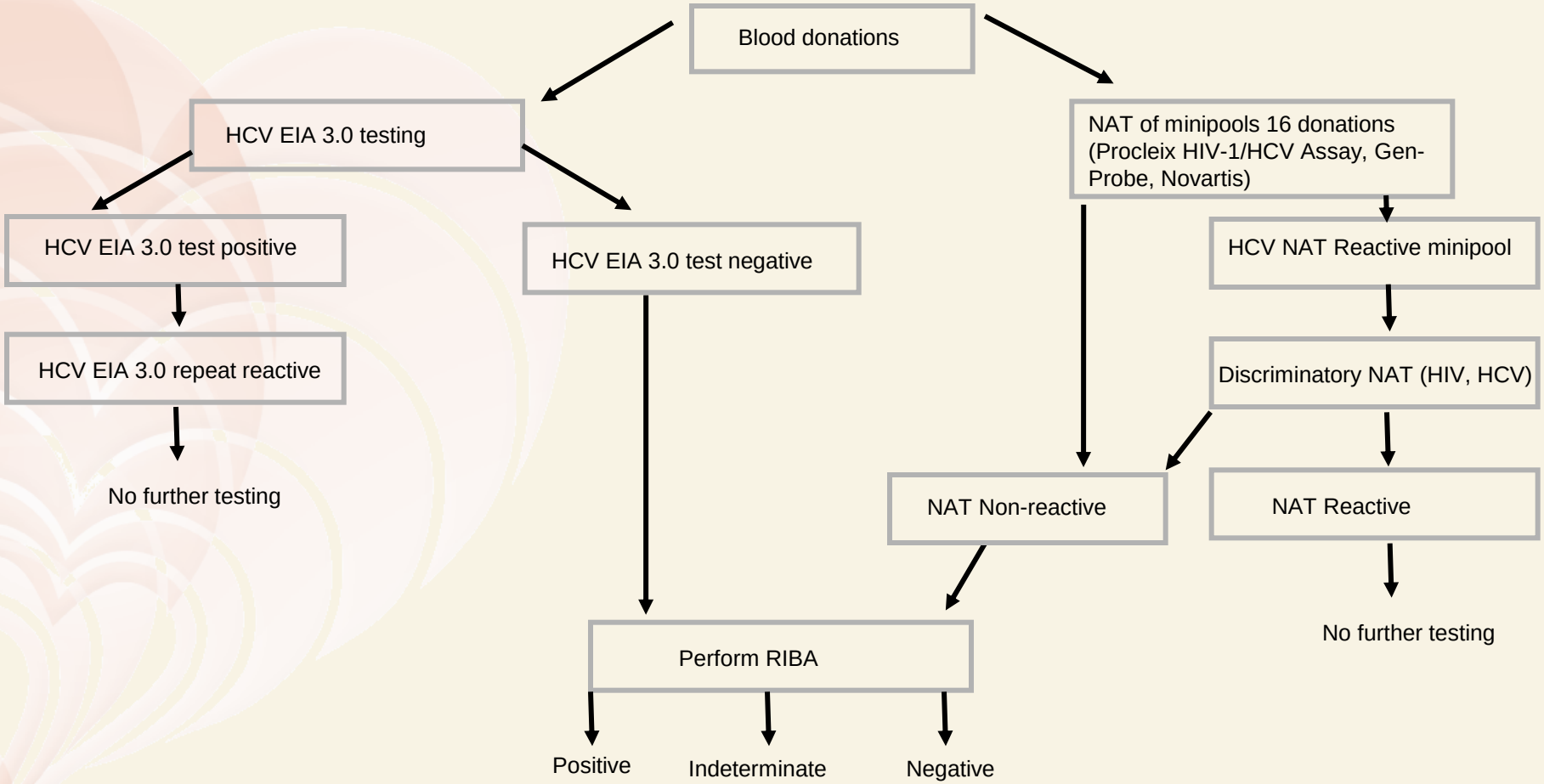
Routine testing for HCV at Blood centers & classification of outcomes

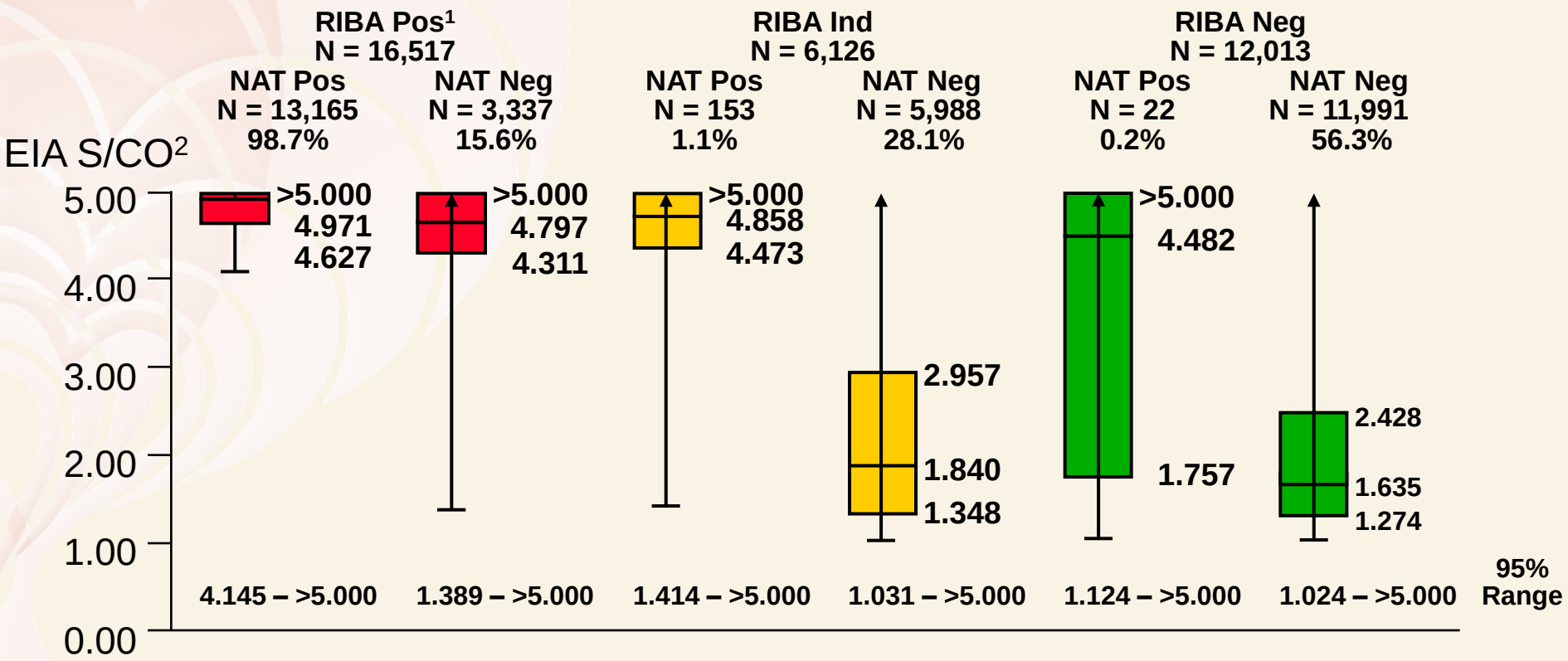


Test result	Disease outcome
NAT RNA -/ EIA -/RIBA -	No HCV Infection
NAT RNA -/ EIA +/RIBA +	HCV confirmed serology but RNA negative indicating presumptive clearance
NAT RNA +/ EIA +	Chronic HCV infection
NAT RNA +/EIA -/ RIBA -	Acute HCV before seroconversion

Blood Systems

Selvarajah et al.,
Current Opinion in Hematology,2010

Relationship between 3rd-gen HCV EIA S/Co and RIBA Interpretations among HCV RNA-pos and RNA-neg Donations



Kleinman, et al. TRANSFUSION, 46:695-702, 2005

Blood Systems

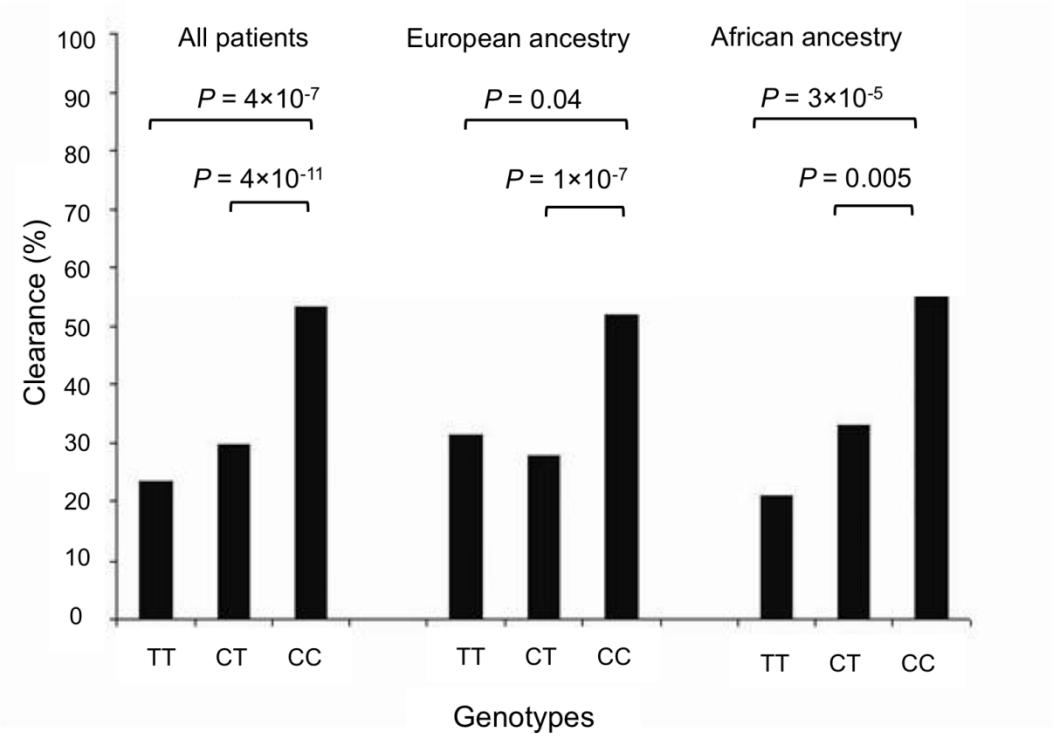
OR Comparing Odds of Being HCV-Seropositive and HCV RNA (MP-NAT)-Negative by Demographic Characteristic

Demographic Characteristic	Unadjusted OR (95 % CI)	OR Adjusted for Age, Sex, and Race and/or Ethnicity
Age (years)		
< 25	1.0	1.0
25 - 34	1.78 (1.09 - 2.90)	2.08 (1.20 - 3.60)
35 - 44	1.51 (0.98 - 2.33)	1.75 (1.07 - 2.87)
45 - 54	1.24 (0.79 - 1.95)	1.48 (0.88 - 2.46)
55 - 64	1.06 (0.54 - 2.09)	1.30 (0.62 - 2.73)
≥ 65	1.50 (0.52 - 4.36)	1.98 (0.66 - 5.98)
Sex		
Male	1.0	1.0
Female	1.21 (0.97 - 1.51)	1.14 (0.90 - 1.45)
Race and / or Ethnicity		
White non-Hispanic	1.0	1.0
Asian	0.34 (0.12 - 0.96)	0.36 (0.13 - 1.01)
Black non-Hispanic	0.64 (0.44 - 0.93)	0.66 (0.45 - 0.96)
Hispanic	1.08 (0.79 - 1.49)	1.08 (0.78 - 1.48)
Other	1.02 (0.58 - 1.80)	1.03 (0.58 - 1.83)

Blood Systems

Busch, et al. TRANSFUSION, 46:469-475, 2006

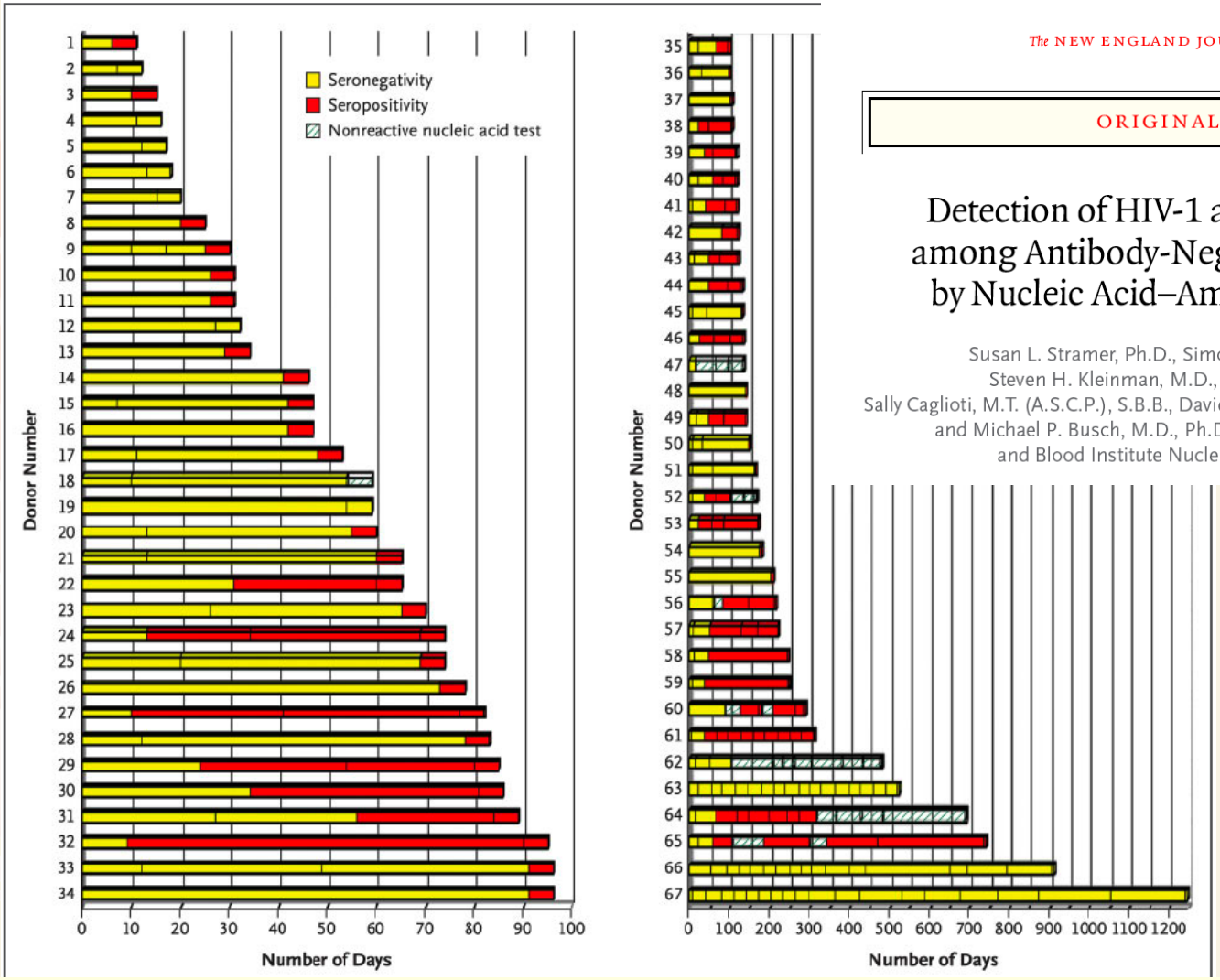
Percentage of HCV clearance by rs12979860 genotype



Individuals with *CC* as opposed to *CT* or *TT* genotypes have a higher chance of clearing the virus spontaneously irrespective of race.

Blood Systems

Thomas et al., Nature: 2009 ; Selvarajah et al., Current Opinion in Hematology, 2010



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Detection of HIV-1 and HCV Infections among Antibody-Negative Blood Donors by Nucleic Acid–Amplification Testing

Susan L. Stramer, Ph.D., Simone A. Glynn, M.D., M.P.H., Steven H. Kleinman, M.D., D. Michael Strong, Ph.D, Sally Caglioti, M.T. (A.S.C.P.), S.B.B., David J. Wright, Ph.D., Roger Y. Dodd, Ph.D., and Michael P. Busch, M.D., Ph.D., for the National Heart, Lung, and Blood Institute Nucleic Acid Test Study Group

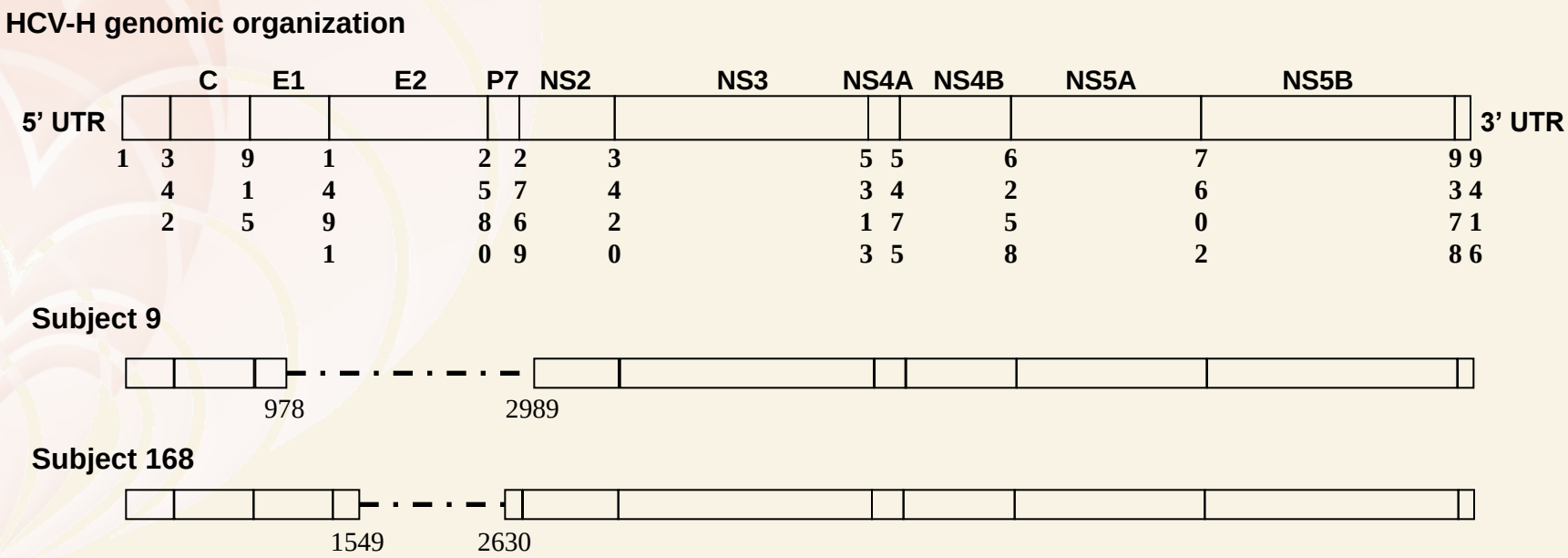
39,721,404 donation tested from 7/99 – 12/05.

139 HCV RNA positive, seronegative (EIA 3.0) donors detected.

90 HCV RNA only donors enrolled. Average time seroconversion: 35 days.

3 remained persistently seronegative with all serological assays.

Large deletion in E1-NS2 in sero-silent carriers



Bernardin et al. Virology 2007

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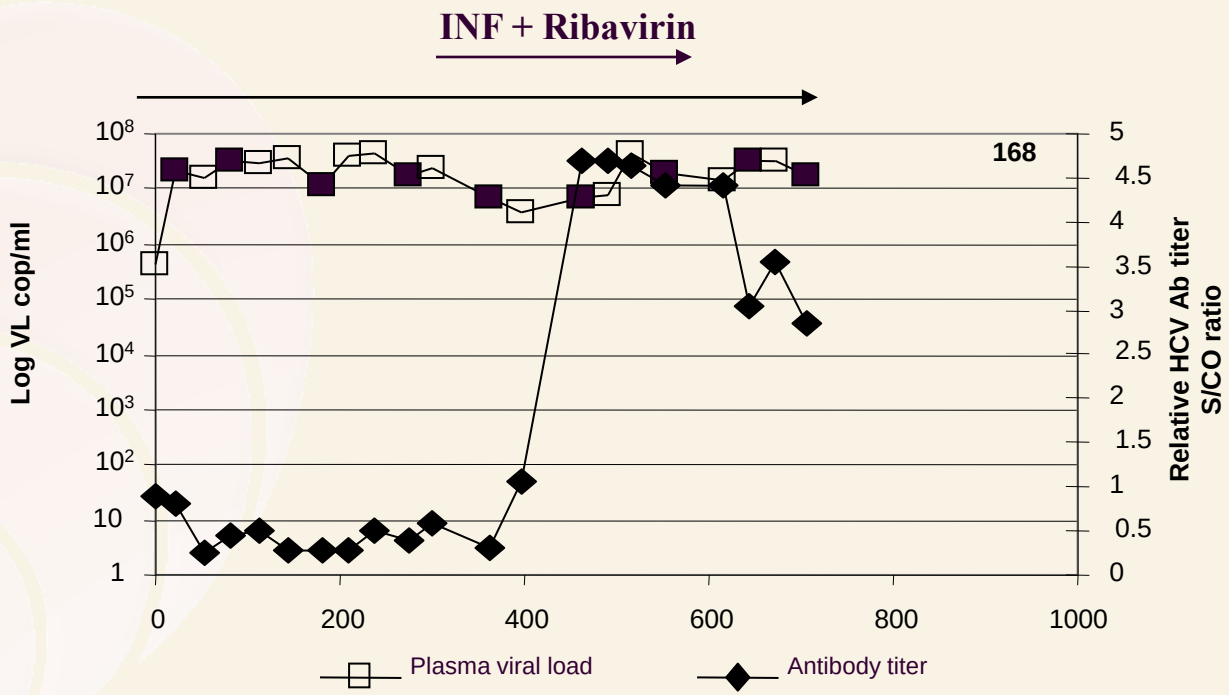
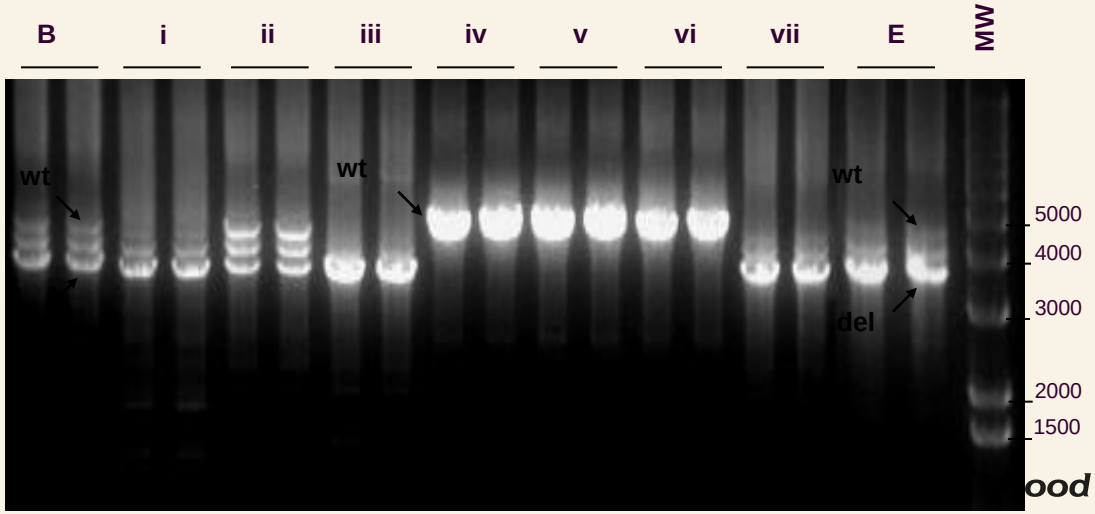
Deleted HCV quasispecies in sero-silent carrier



TN168 (1a)



Bernardin et al. Virology 2007

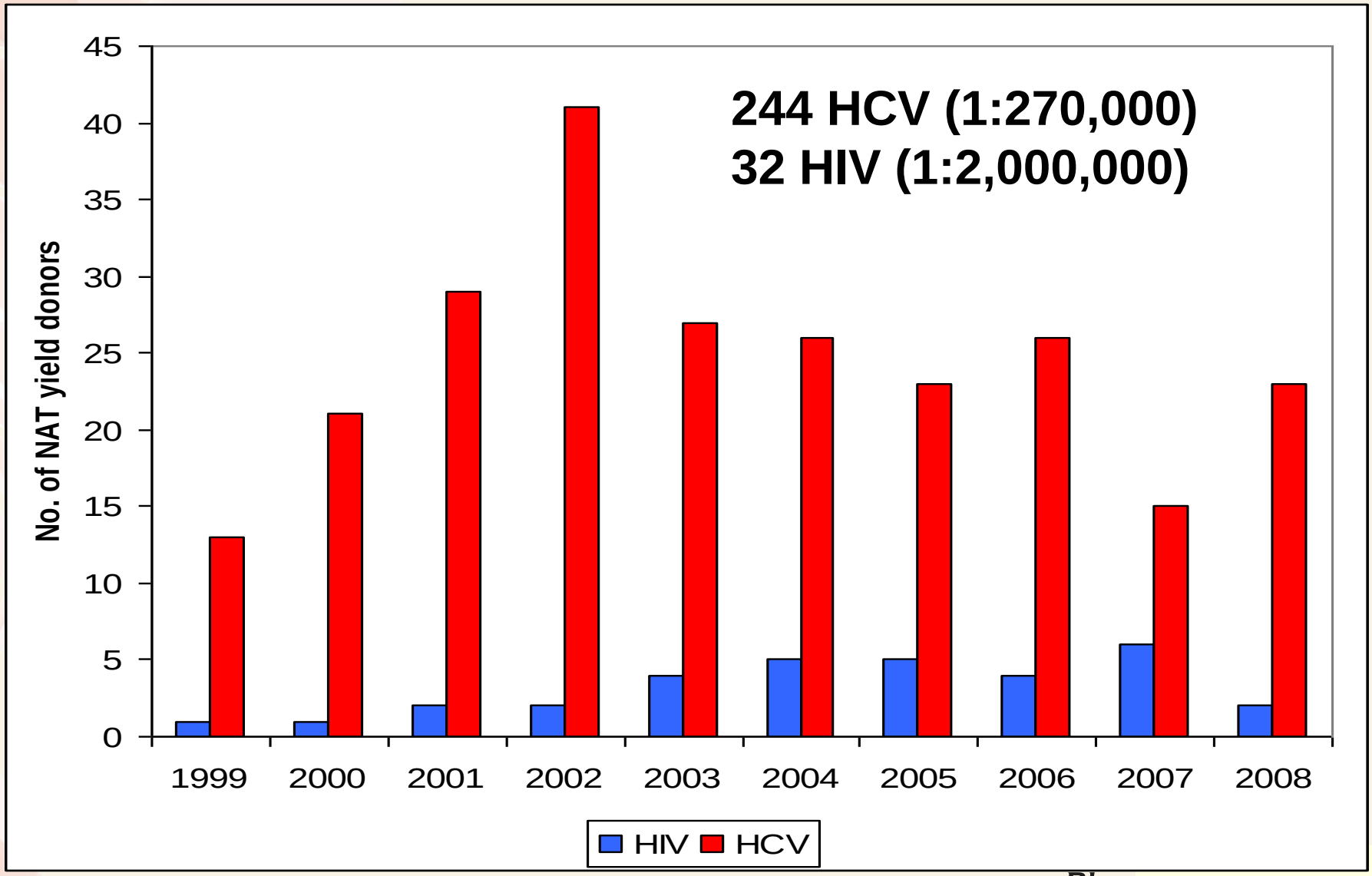
Risk factors for HCV infection among blood donors confirmed to be positive for the presence of HCV RNA and not reactive for the presence of anti-HCV

TABLE 2. Comparison of cases and controls for history of known and potential risk factors for HCV infection: univariate analysis

History in the 6 months before donation	Cases (n = 65)*†	Controls (n = 225)*†	OR (95% CI)	p value
IDU	19 (29.2)	0 (0.0)	Undefined	<0.00001‡
Snort drugs	13 (20.0)	0 (0.0)	Undefined	<0.00001‡
Sex with an IDU	12 (18.5)	4 (1.8)	12.5 (3.6-54)	0.00006‡
Friends use street drugs	25 (38.5)	15 (6.7)	8.8 (4.2-18)	<0.00001‡
Reside with an IDU	5 (7.7)	0 (0.0)	Undefined	0.0005‡
Jail	17 (30.9)	26 (12.0)	3.3 (1.6-6.6)	0.0006‡
Two or more sexual partners	14 (21.5)	11 (4.9)	5.3 (2.3-13)	0.00007‡
Medical or dental job (frequent blood contact)	6 (9.2)	8 (3.6)	2.8 (0.8-9.4)	0.09
Public safety job (frequent blood contact)	2 (3.1)	8 (3.6)	1.0 (0.1-5.4)	1.00
Sex partner had hepatitis	5 (7.7)	4 (1.8)	4.6 (1.0-24)	0.03
Nonsexual contact with someone diagnosed with hepatitis‡	5 (7.6)	6 (2.7)	3.0 (0.7-12)	0.07
Had a sexually transmitted disease	4 (6.2)	0 (0)	Undefined	0.002
Had a tattoo	3 (4.6)	1 (0.5)	11 (0.8-566)	0.04
Had body piercing	3 (4.6)	5 (2.2)	2.1 (0.3-11)	0.38
Had dental work	23 (35.4)	87 (38.8)	0.9 (0.5-1.5)	0.61
Was hospitalized	5 (7.7)	5 (2.2)	3.7 (0.8-16)	0.05
Had same day surgery	6 (9.2)	14 (6.3)	1.5 (0.5-4.5)	0.41
Had a medical and/or surgical procedure	14 (21.5)	32 (14.3)	1.6 (0.8-3.3)	0.16
Other blood exposure				
At accident site	4 (6.2)	3 (1.3)	4.9 (0.8-34)	0.05
In a fight	5 (7.7)	5 (2.2)	3.7 (0.8-16)	0.05
By a bite	3 (4.6)	0 (0.0)	Undefined	0.01
During a haircut	15 (23.1)	31 (13.8)	1.9 (0.9-3.9)	0.11
During a manicure§	6§ (20.0)	4§ (3.8)	5.2 (1.1-27)	0.02
Travel outside the US	1 (1.5)	15 (6.7)	0.2 (0.01-1.5)	0.13
Received hepatitis B vaccine	21 (32.3)	55 (24.6)	1.5 (0.8-2.7)	0.21
Previous history of hepatitis	1 (1.5)	4 (1.8)	0.9 (0.02-10)	1.00
History > 6 months before donation‖				
IDU	2 (4.9)	1 (0.5)	10.9 (0.6-647)	0.07
Injecting steroids	2 (3.5)	1 (0.5)	7.6 (0.4-448)	0.12
Intranasal drug use	8 (17.4)	14 (6.6)	3.0 (1.0-8.2)	0.04
Jail	17 (30.9)	26 (12.0)	3.3 (1.6-6.6)	0.0006 ‡

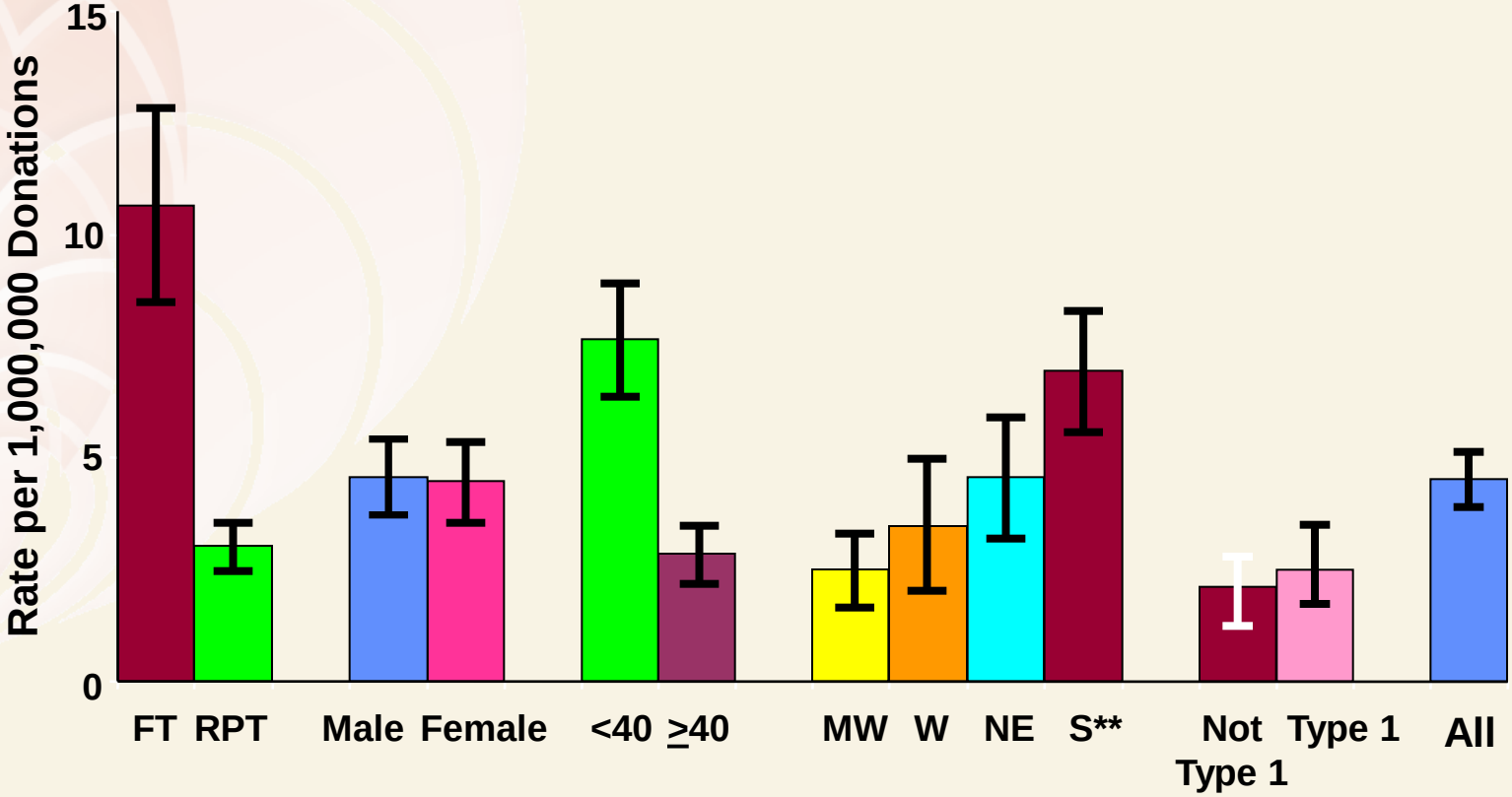
S.L. Orton, S.L. Stramer, R.Y. Dodd, and M.J. Alter

HIV and HCV NAT RNA +/Ab – "Yield" Donors, ARC: 1999-2008



Blood

Rates of HCV NAT Positive Donors by Demographic/Regional Characteristics



Dtn Status p=0.0022

Gender p=0.90

Donor Age (Years) p<0.001

Collection Area p=0.01

Genotype p=0.074

Blood Systems

Why Conduct Surveillance for Variants of Transfusion-Transmissible Viruses in Donors?

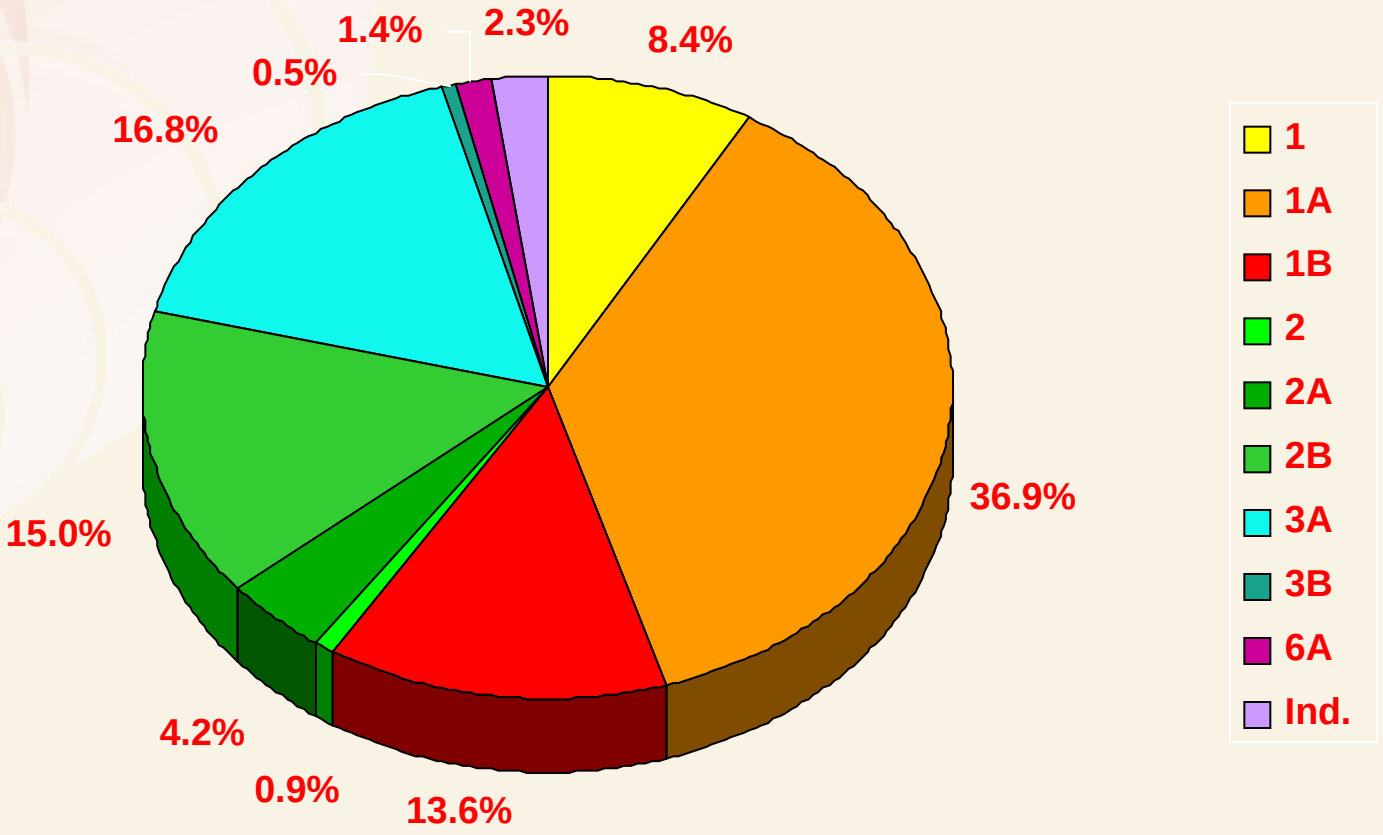
- Assure screening, diagnostic and supplemental assays detect circulating TTV strains
  - Assays presently based on prototype strains
  - Numerous studies have demonstrated failure of assays to sensitively detect and accurately quantify divergent subtypes
  - Documentation of divergence in donor pool will lead to accelerated development and licensure of robust serological and NAT assays for donor, diagnostic and clinical management
  - Detection of variants in blood donors allows access to plasma components for use in test development, evaluation and QC

- Public health implications - characterize & monitor recently transmitted viruses, including drug resistant phenotypes, in large convenience but representative subgroup of population

- Pathogenesis and Vaccine implications – Detailed knowledge of characteristics of “transmitted viruses” informs HIV/HCV vaccine development and documents rates and types of HBV vaccine escape mutants

Blood Systems

HCV NAT Yield Cases by Genotype



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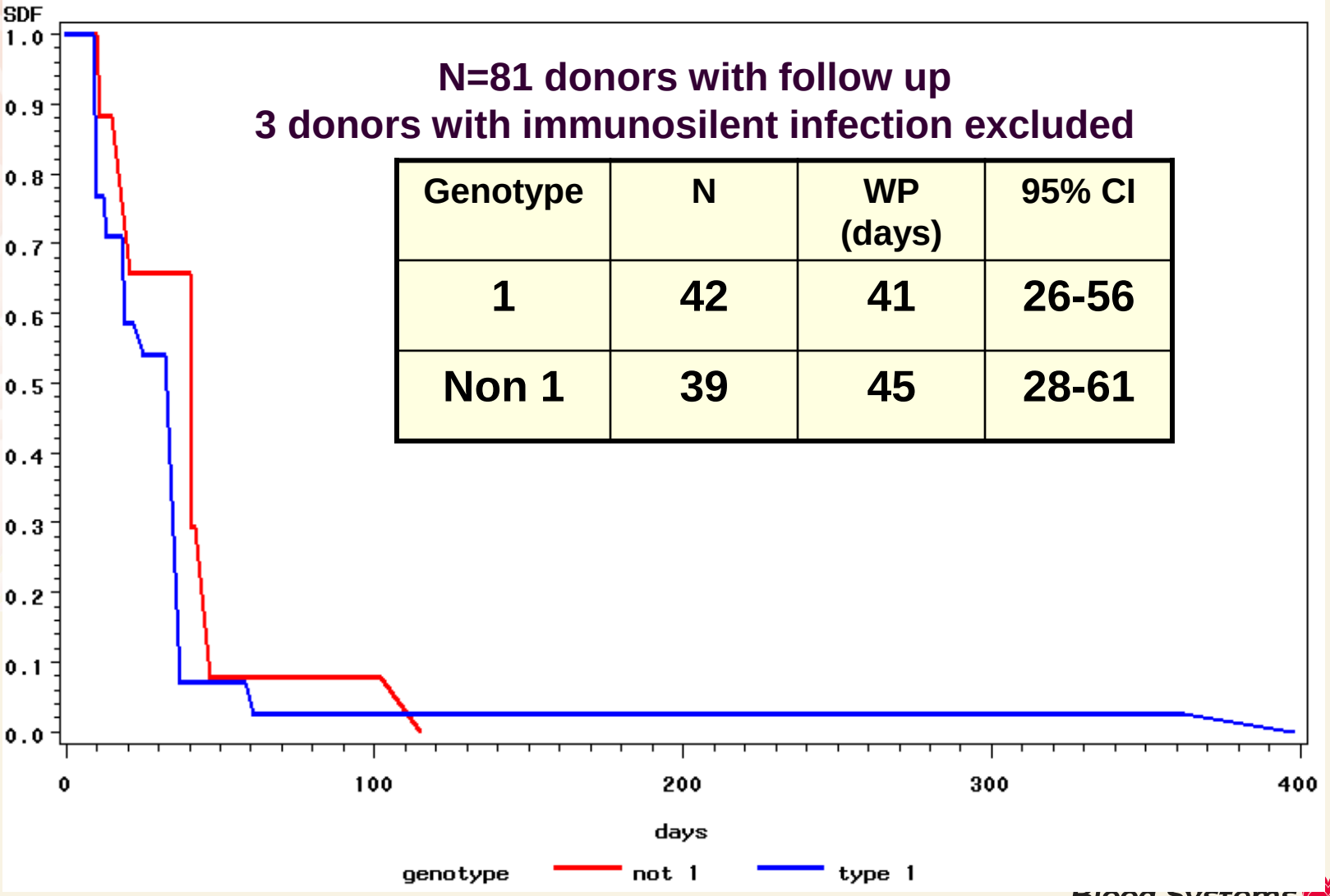
Time to HCV Seroconversion by Genotype



N=81 donors with follow up
3 donors with immunosilent infection excluded

Genotype	N	WP (days)	95% CI
1	42	41	26-56
Non 1	39	45	28-61

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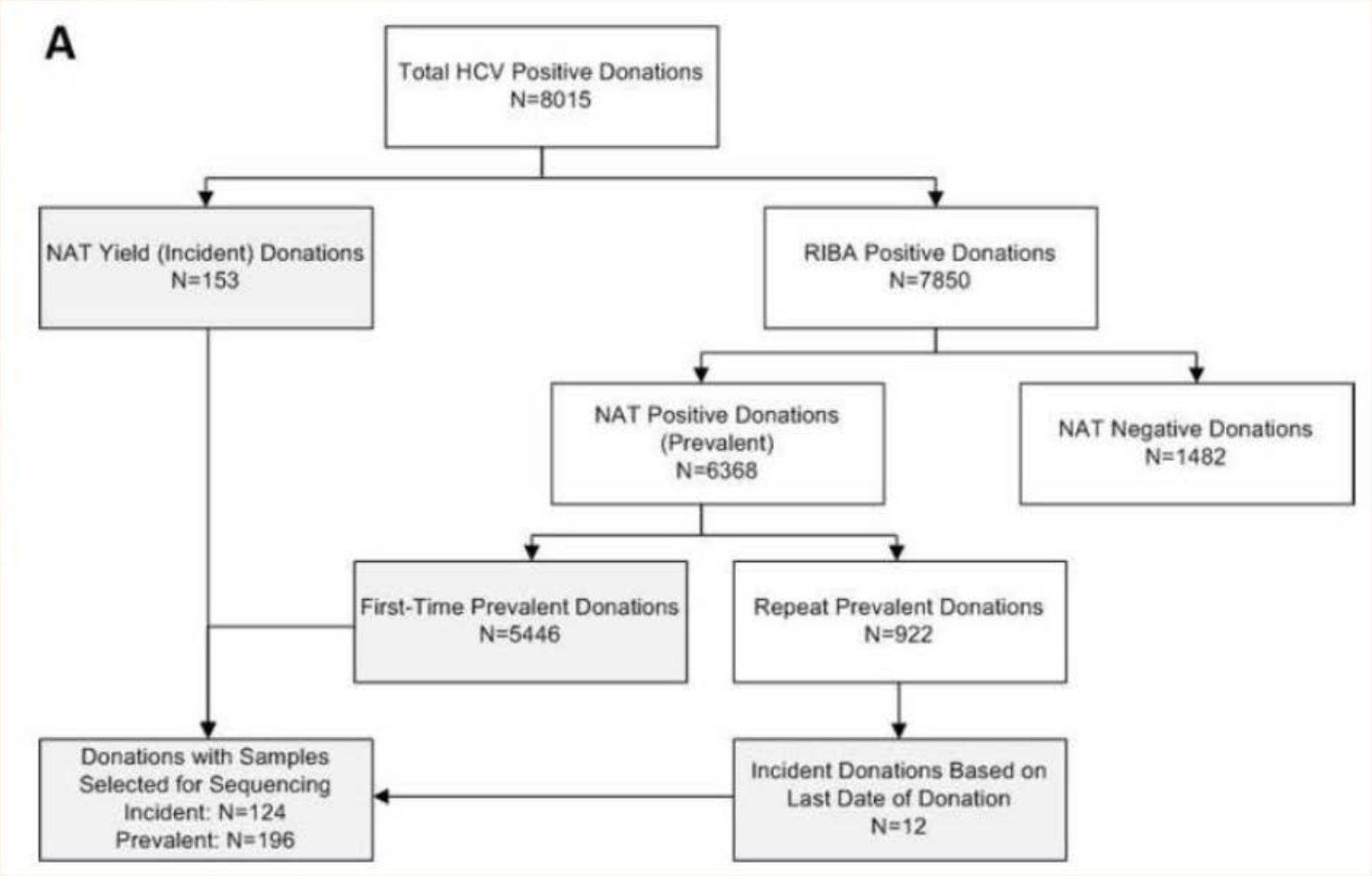
The Journal of Infectious Diseases

Genetic diversity of recently acquired and prevalent HIV, HBV and HCV infections in US blood donors



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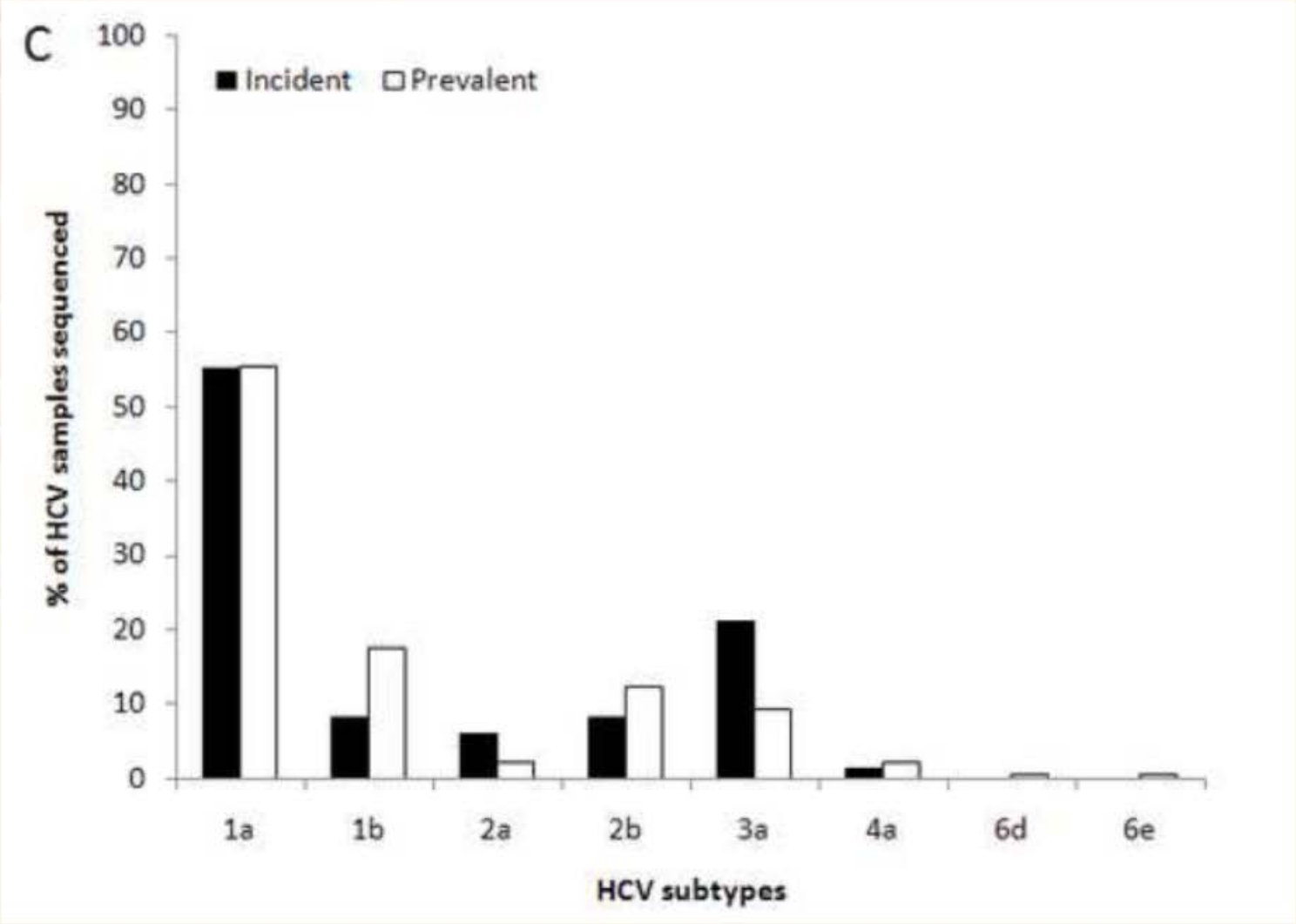

Blood Systems

NHLBI REDS-II Study Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors

- Interview all HIV and HTLV confirmed positive donors as possible during the 1-year study period
- Interview a sample of 500 HCV and 500 HBV confirmed positive donors

- Compare risk factors reported by confirmed positive donors (cases) to those reported by comparison groups of false reactive donors (controls)
  - False reactive donors are defined as screening test reactive, but confirmatory test negative
  - Excludes indeterminate donors

Interview Content

- Content Domains
  - Demographic data
  - Donor motivations (brief)
  - Risk factors and behaviors (open and closed-ended questions)
  - Donor quality of life (EQ-5D)
    - Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression
- Common Risk Factors
  - Sexual exposures (life time, last 5 years, last year)
  - Injected drug use (life time, last year)
  - Exchanging money or drugs for sex (life time, last year)
  - Family history/from endemic area
- Less Common Risk Factors (life time, last year)
  - Non-injected drug use
  - Tattoos, piercing and related
  - Incarceration/detention facilities
  - Medical procedures
    - Blood/transplant
    - Endoscopy/colonoscopy
  - Needlestick injuries

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Blood Systems

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TTVS

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E Operskalski

NHLBI

G Nemo

S Glynn

H Alter

ORIGINAL RESEARCH

Prevalence, incidence, and residual risk of human immunodeficiency virus and hepatitis C virus infections among United States blood donors since the introduction of nucleic acid testing

Shimian Zou, Kerri A. Dorsey, Edward P. Notari, Gregory A. Foster, David E. Krysztof, Fatemeh Musavi, Roger Y. Dodd, and Susan L. Stramer

TRANSFUSION 2010;50: in press

BLOOD DONORS AND BLOOD COLLECTION

Current incidence and residual risk of hepatitis B infection among blood donors in the United States

Shimian Zou, Susan L. Stramer, Edward P. Notari, Mary C Kuhns, David Krysztof, Fatemeh Musavi, Chyang T. Fang, and Roger Y. Dodd

TRANSFUSION 2009;49:1609-1620.

Blood

Outline

- Recent studies using TTVS repository
  - rate and correlates of transmission by Ab+ transfusions
  - timing and correlates of resolution of viremia
- Studies of plasma donor panels
  - acute viral dynamics and time to SC
  - quasispecies complexity of initial innoculum
  - infectivity of HCV during the window phase
- Studies of NAT yield donors and HCV incidence
  - demographics & genotypes of recently transmitted HCVs
  - development of strategies for cross-sectional incidence
  - frequency & mechanism of “serosilent” and “occult” carriers
- Studies of Ab+ donors and spontaneous clearance
  - long-term morbidity and morality
  - host genetic and other correlates of clearance

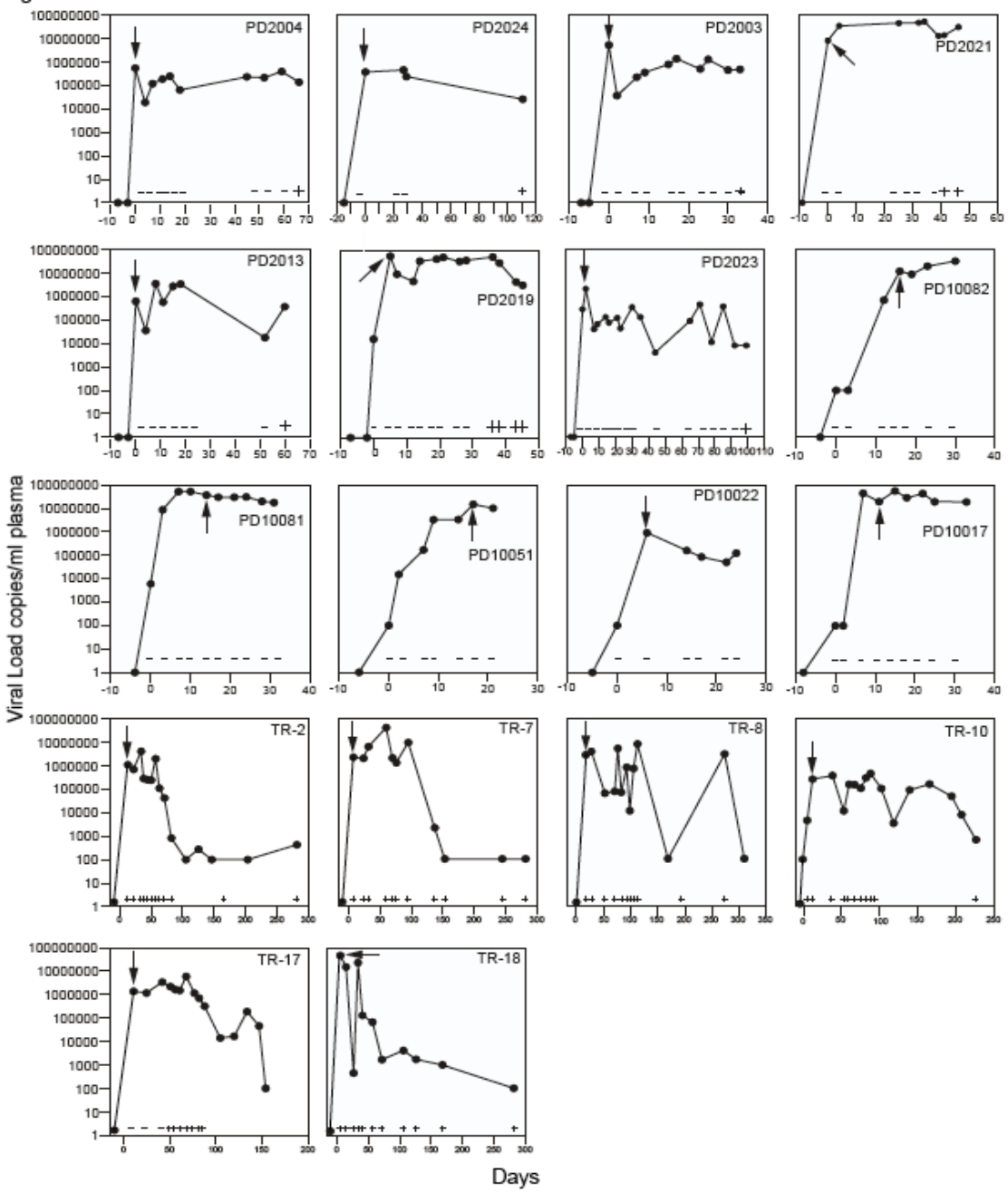
Blood Systems

Genetic analyses of the initial HCV quasispecies in infected plasma donors and transfusion recipients

Does a single or multiple infectious particles get transmitted and initiate infection?

- More diverse innoculum = greater chance of immune/drug escape mutations.
- Acute HIV typically homogeneous, one rationale for early ART

Figure 1

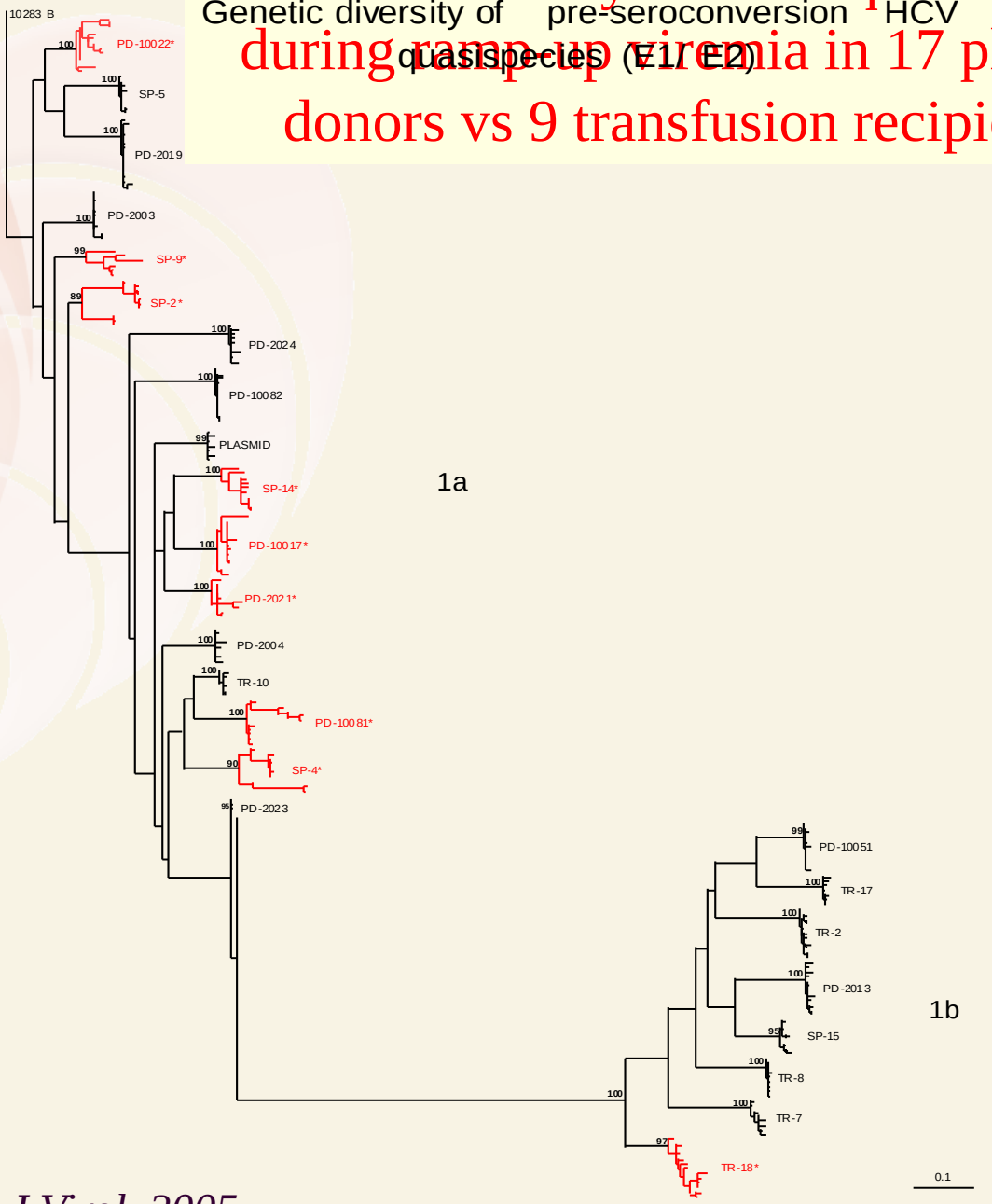


Herring et al.
J Virol, 2005

d Systems

Genetic diversity of HCV quasispecies during ramp-up viremia in 17 plasma donors vs 9 transfusion recipients

Genetic diversity of pre-seroconversion HCV quasispecies (E1/ E2)



Herring et al. J Virol, 2005

Blood Systems

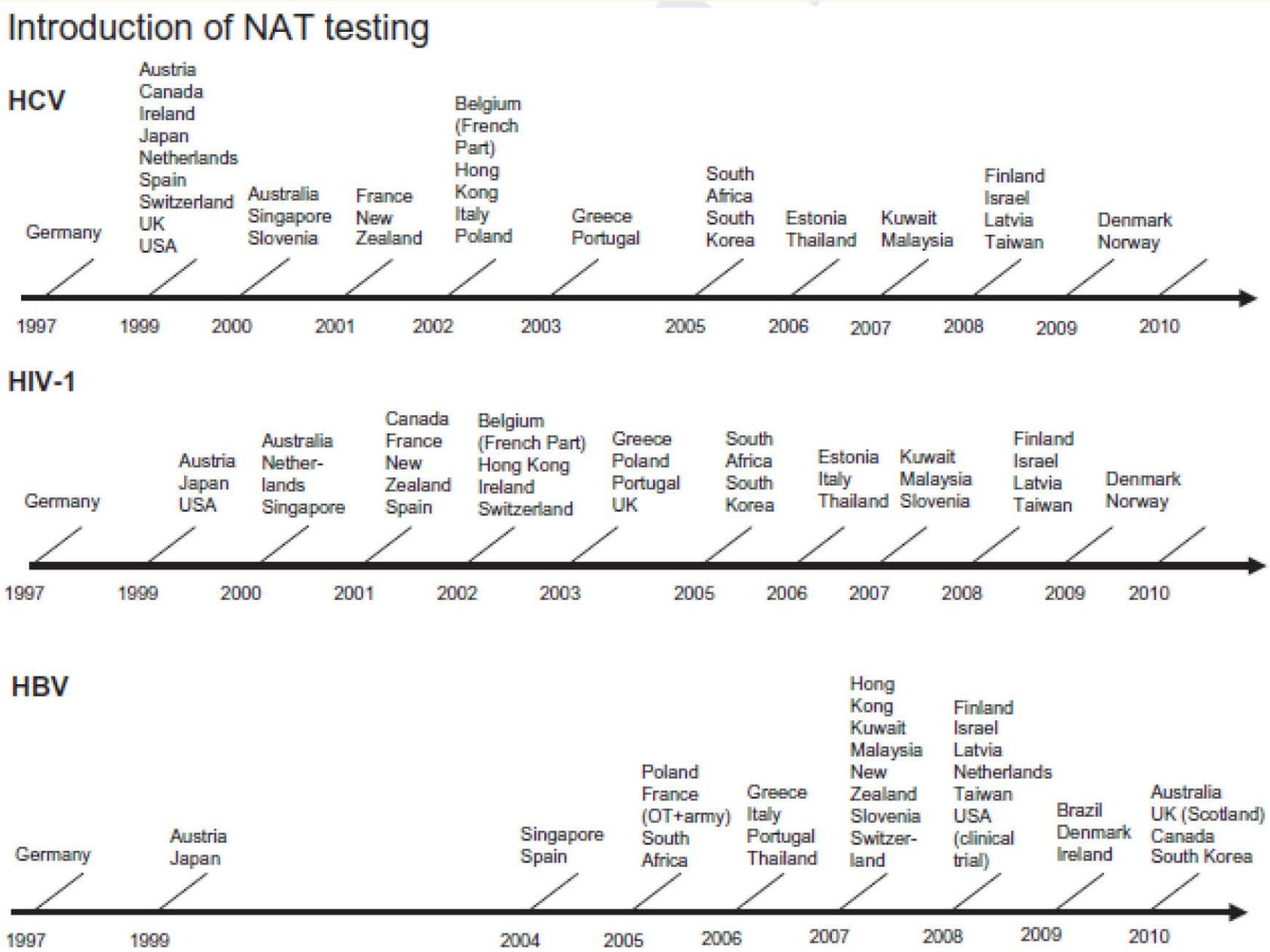


Fig. 1 Introduction of nucleic acid amplification technology (NAT) testing.

HCV NAT Yield per Country

Region / Country	screened donations since implementation of HCV NAT	HCV NAT only positives	yield HCV NAT / million
Africa			
South Africa	2,202,295	4	1.82
Asia - Pacific			
Australia	9,282,841	23	2.48
Hong Kong	1,288,092	0	0
Israel	283,003	0	0
Kuwait	103,000	0	0
Malaysia	208,134	9	43.24
New Zealand	1,428,746	0	0
Singapore	694,967	6	8.63
South Corea	8,843,237	16	1.81
Europe			
Austria	2,015,609	3	1.49
Belgium-French Part	1,279,756	0	0
Estonia	83,664	2	23.91
Finland	277,997	0	0
France	19,300,000	12	0.62
Germany	42,915,877	29	0.68
Greece	1,173,002	7	5.97
Ireland	1,624,845	0	0
the Netherlands	9,300,000	1	0.11
Poland	7,647,878	83	10.85
Portugal	1,003,047	6	5.98
Slovenia	672,113	2	2.98
Spain	10,220,514	22	2.15
UK	25,663,340	14	0.55
North America			
Canada	10,967,559	3	0.27
USA	75,950,280	296	3.90

Blood Systems

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Testing Strategy To Identify Cases of Acute Hepatitis C Virus (HCV) Infection and To Project HCV Incidence Rates[▽]

Kimberly Page-Shafer,[1] Brandee L. Pappalardo,[2]† Leslie H. Tobler,[2] Bruce H. Phelps,[3]‡ Brian R. Edlin,[1,4] Andrew R. Moss,[1] Teresa L. Wright,[1,5]§ David J. Wright,[6] Thomas R. O'Brien,[7] Sally Caglioti,[8] and Michael P. Busch[1,2,8]*

TABLE 2. HCV-viremic seronegative infections, estimated HCV incidence, and observed HCV incidence in sample populations

Population	No. of anti-HCV-negative individuals (N_{sn})	No. of anti-HCV-negative/HCV RNA-positive individuals (n_{vsn})	Proportion (95% CI) of anti-HCV-negative/HCV RNA-positive individuals (per 1,000)	Projected incidence rate (95% CI) (per 100 person-yr)	Observed incidence rate (95% CI) (per 100 person-yr)
Blood donors	4,620,687	29	0.0059 (0.0032, 0.0084)	0.0054 (0.0036, 0.0072)	0.0028 (0.0021, 0.0034)
VA patients	835	1	1.20 (0.03, 6.65)	0.86 (0.02, 7.1)	
Young IDU	618[a]	34	49.0 (32.8, 72.0)	39.8 (25.9, 53.7)	33.4 (28.0, 39.9)
Older IDU					
≥10 yr of exposure	72	4	55.6 (15.3, 136.2)	39.8 (9.1, 115.0)	15.4 (9.9, 22.9)
<10 yr of exposure	75	7	93.3 (38.4, 182.9)	66.9 (23.3, 153.6)	33.1 (23.1, 45.7)
Total	147	11	74.8 (37.9, 129.9)	53.7 (23.4, 108.8)	22.5 (17.2, 28.8)

[a] A total of 618 (90.5%) anti-HCV-negative samples, as tested by EIA 3, were available from 683 HCV-negative samples.

Blood Systems

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Distinguishing Acute from Chronic and Resolved Hepatitis C Virus (HCV) Infections by Measurement of Anti-HCV Immunoglobulin G Avidity Index[▽]

S. Klimashevskaya,[1,2] A. Obriadina,[2] T. Ulanova,[2] G. Bochkova,[2] A. Burkov,[2] A. Araujo,[1] Susan L. Stramer,[3] Leslie H. Tobler,[4] Michael P. Busch,[4] and Howard A. Fields[1]*

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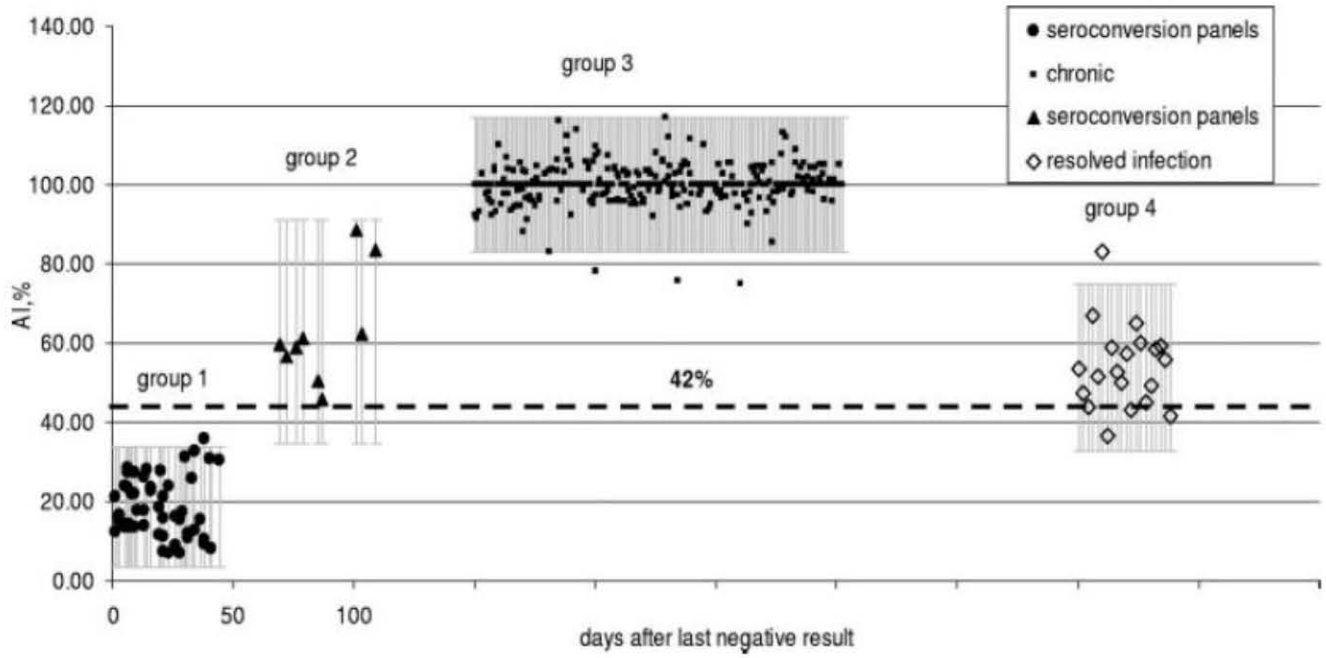

Blood Systems

Genetic association studies on *IL-28B* gene polymorphism and HCV clearance

References	Country	Number of patients	Ethnic origin	HCV Disease outcome	SNP identified
Ge et al. [39]	North America	1137	African-Americans 191 European-Americans 871 Hispanics 75	Treatment-induced (IFN-α + ribavirin) clearance and chronics	rs12979860 (~ 3kb upstream of IL-28B) linkage disequilibrium with rs 8099917
Suppiah et al. [40]	Australia Europe	848	Australians 293 European 555	Treatment-induced (IFN-α + ribavirin) clearance and chronics	rs8099917 (~8kb upstream of IL-28B) 16 other SNPs identified
Tanaka et al. [41]	Japan	314	Japanese 314	Treatment-induced (IFN-α + ribavirin) clearance and chronics	rs8099917 (~8kb upstream of IL-28B) rs12980275 rs1188122 rs8105790
Thomas et al. [42]	North America	1008	African-Americans 290 European-Americans 642 Other 76	Spontaneous clearance and chronics	rs12979860 (~ 3kb upstream of IL-28B)
Rauch et al. [43]	Switzerland	1362	Swiss whites 1362	Spontaneous clearance, Treatment-induced clearance and chronics	rs8099917 (~8kb upstream of IL-28B)

Blood Systems

Selvarajah et al., Current Opinion in Hematology, 2010

Advantages and limitations of using blood center derived HCV positive samples for large-scale studies

Advantages

- Systematic screening of a cross-section of the society for HCV prevalence
- Large pool of first-time (FT) donors infected with HCV
- Donor samples give relevant information on age, gender, ethnicity and infectious disease screening results
- HCV routine testing using NAT, EIA and RIBA help identify HCV disease outcomes such as acute, spontaneously cleared and chronically infected individuals
- Routine blood donor screening also tests for HIV allowing the removal of these samples from genetic studies if necessary
- HCV treatment-induced clearance or treatment failure can be studied with a new IRB approval in a separate study that is designed as a follow-up study of FT donors screened by blood centers

Limitations

- Only a snap shot of HCV infection
- Future recalls will require IRB approval
- HCV treatment-induced clearance or treatment failure cannot be studied without new IRB approval and a renewed source of funding

Blood Systems

HCV Morbidity: Study Population

Characteristic	HCV Positive n = 312		HCV Neg n = 446	
Female	146	(47%)	193	(43%)
Male	167	(53%)	253	(57%)
Mean Age at Survey	51.4		52.2	
Mean Age at Donation	40.3		40.7	
Mean Index Donation	1996		1995	
Race/Ethnicity				
White	257	(82%)	373	(84%)
Black	14	(4%)	7	(2%)
Hispanic/Latino	27	(9%)	39	(9%)
Asian	1	(0%)	10	(2%)
Other	12	(4%)	16	(4%)

Blood Systems

Cardiovascular Outcomes & Risks

Characteristic	HCV Pos n = 312	HCV Neg n = 446	OR (95% CI)
Myocardial Infarction	13 (4%)	10 (2%)	1.76 (0.76-4.08)
Angina	13 (4%)	16 (4%)	1.09 (0.51-2.29)
Stroke	9 (3%)	7 (2%)	1.63 (0.56-4.80)
Current smoker	108 (38%)	53 (12%)	4.41 (3.03-6.41)
High Cholesterol	61 (20%)	111 (27%)	0.66 (0.46-0.94)
Hypertension	72 (24%)	129 (31%)	0.68 (0.48-0.95)
Family Hx CAD	37 (12%)	26 (6%)	2.05 (1.21-3.47)

Blood Systems

“Lifestyle” Outcomes

Characteristic	HCV Pos n = 312	HCV Neg n = 446	OR (95% CI)
Psychiatric Dx	95 (31%)	65 (15%)	2.59 (1.81-3.70)
Substance abuse Dx	79 (25%)	26 (6%)	5.47 (3.42-8.77)
Drug overdose	44 (14%)	12 (3%)	5.92 (3.07-11.41)
Motor vehicle accident	94 (30%) `	58 (13%)	2.87 (1.99-4.14)
Violent wound	18 (6%)	11 (2%)	2.41 (1.12-5.18)
Fall/Work accident	55 (18%)	43 (10%)	.00 (1.30-3.07)

Blood Systems