

Ireland: Donor Screening Results

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HEV Blood Donor Prevalence

	Anti-HEV IgG Seroprevalence (Wantai)	HEV RNA Prevalence	HEV RNA Testing format	Reference
England	12%	1 : 2,848	MP-24	Hewitt <i>et al.</i> (2014) Beale <i>et al.</i> (2011)
France	24%	1 : 2,218	MP-96	Gallian <i>et al.</i> (2014)
SW France	52%			Mansuy <i>et al.</i> (2011)
Netherlands	27%	1 : 2,671	MP-48	Slot <i>et al.</i> (2013)
		1 : 762	MP-96	Hogema <i>et al.</i> (2016)
Denmark	20%			Holm <i>et al.</i> (2015)
		1: 2,331	ID	Harritshoj <i>et al.</i> (2016)
Spain	20%	1 : 3,333	ID	Sauleda <i>et al.</i> (2015)
Canada	6%	0 : 14,000	MP	Fearon <i>et al.</i> (2014)
USA		1 : 9,500	ID	Stramer <i>et al.</i> (2016)
	16%			Xu <i>et al.</i> (2013)
Australia	6%			Shrestha <i>et al.</i> (2014)
		1:14,799	ID	Shrestha <i>et al.</i> (2016)
Ireland	5%	1: 5,000	ID	O’Riordan <i>et al.</i> (2016)

HEV: To screen or not to screen?

- Fulfills criteria?:
 - Asymptomatic infection of a donor
 - Proven transfusion transmission
 - Potential for significant disease in some transfusion recipients
(Approx 60 % of platelet¹ & 30% RBCs² –haematological & non haematological malignancies in the UK)
 - Considerable cost
- Liability issues for IBTS
- Selective vs universal screening - little clinical awareness of HEV
- Medical Advisory Committee & Board of IBTS
- Funding (DOH) for initial 3 years; commenced ID-NAT on 4th Jan 2016

1. Charlton et al. *Transfus Med* 2014;24:213-8

2. Tinegate et al. *Transfusion* 2016;56:139-45

Procleix Panther system



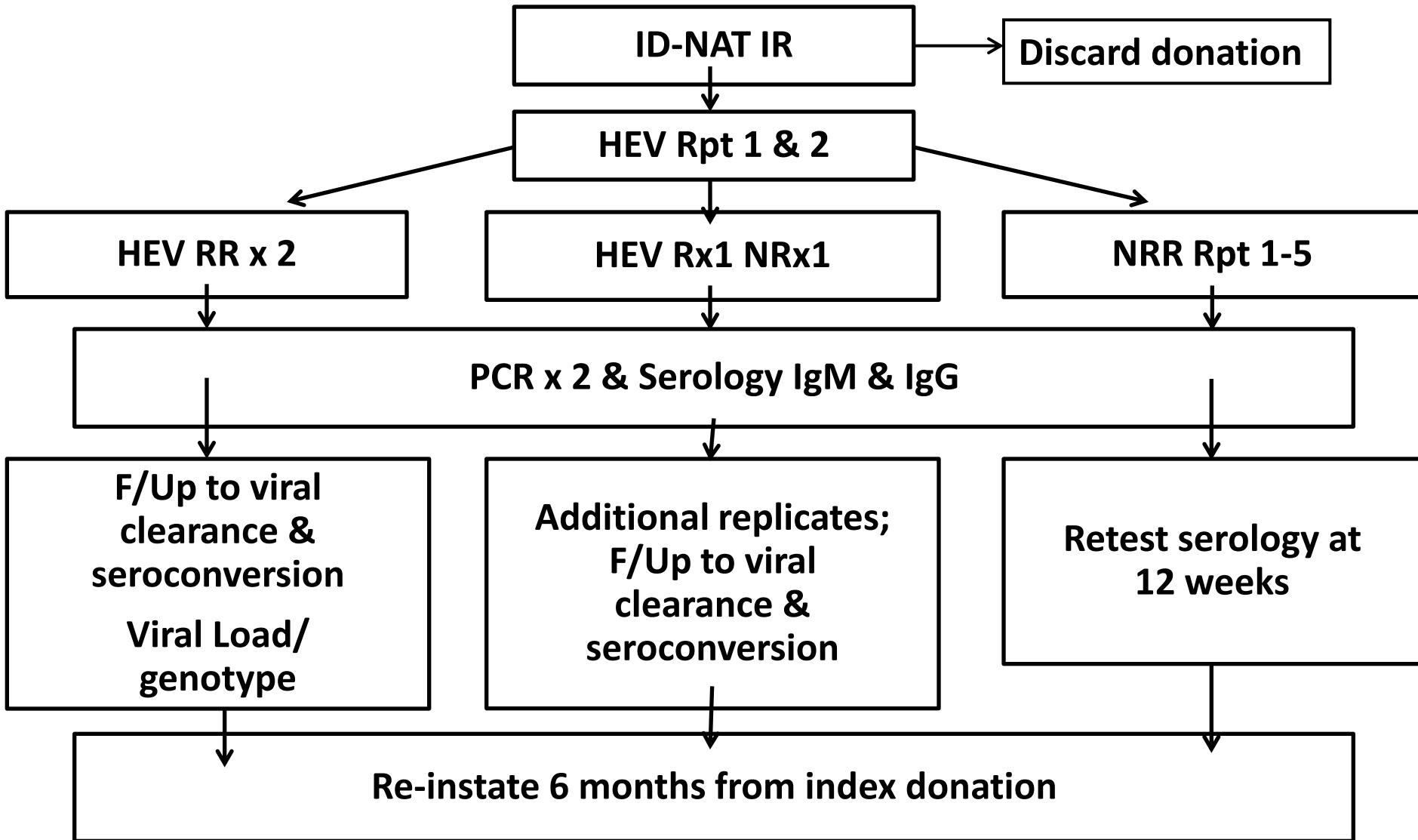
ID NAT	Assay
HIV-1/2 HCV HBV	Procleix Ultrio Elite
WNV	Procleix WNV
HEV	Procleix HEV

Sensitivity of Procleix HEV assay Panther

- 50% and 95% LoD testing using WHO IS for HEV RNA (n=74 replicates across 5 instruments)
- Dilution series: 90, 30, 10, 3, 1 IU/mL

HEV WHO IS 6329/10	HEV Product Insert (Grifols; n=162)	IBTS HEV (n= 74)
50% LoD (IU/mL) (95% CI)	2.02 (1.71 – 2.32)	1.79 (1.46 – 2.16)
95% LoD (IU/mL) (95% CI)	7.89 (6.63 – 9.83)	8.25 (6.12 – 12.91)

HEV ID-NAT Screening Algorithm



HEV Confirmatory Testing

- Nat Virus Ref Lab - Serology-IgM & IgG Wantai
 - RealStar RT-PCR kit, Altona
- Public Health England, Colindale:
 - Viral load ¹
 - Sequencing across part of ORF2²
- Sanquin Blood Supply foundation:
 - Input vol of 9.6 mL LLD-3-4 IU/mL³
 - Sequencing of 285-& 304-bp fragments of ORF1 and ORF2 region ⁴

1. *Ijaz et al, J Infect Dis 2005;192:1166-72*

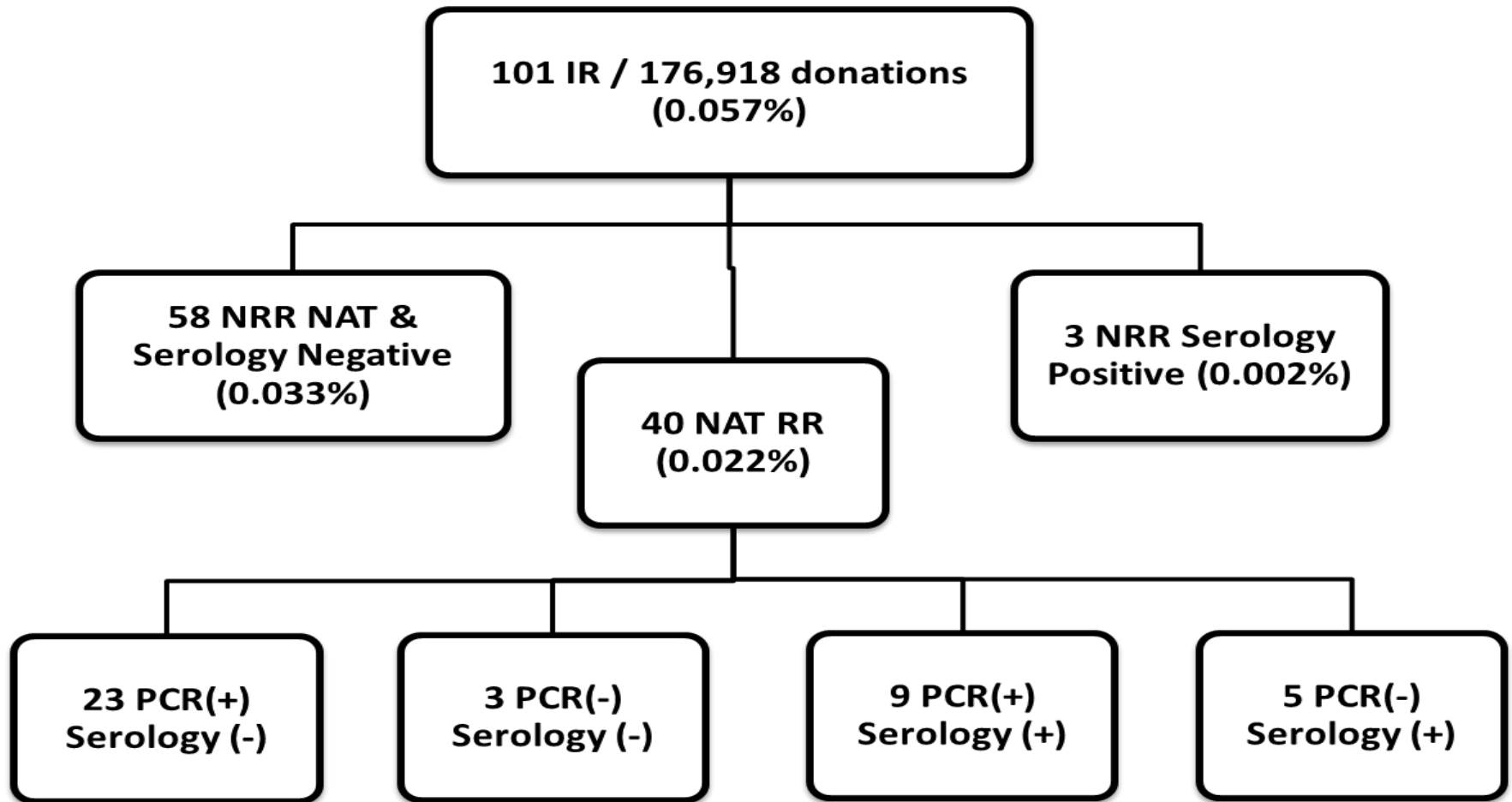
2. *Garson et al, J Virol Methods 2012;186:157-60*

3. *Hogema et al, Transfusion 2016;56:722-728*

4. *Van der Poel et al, Emerg Infect Dis 2001;7:970-6*

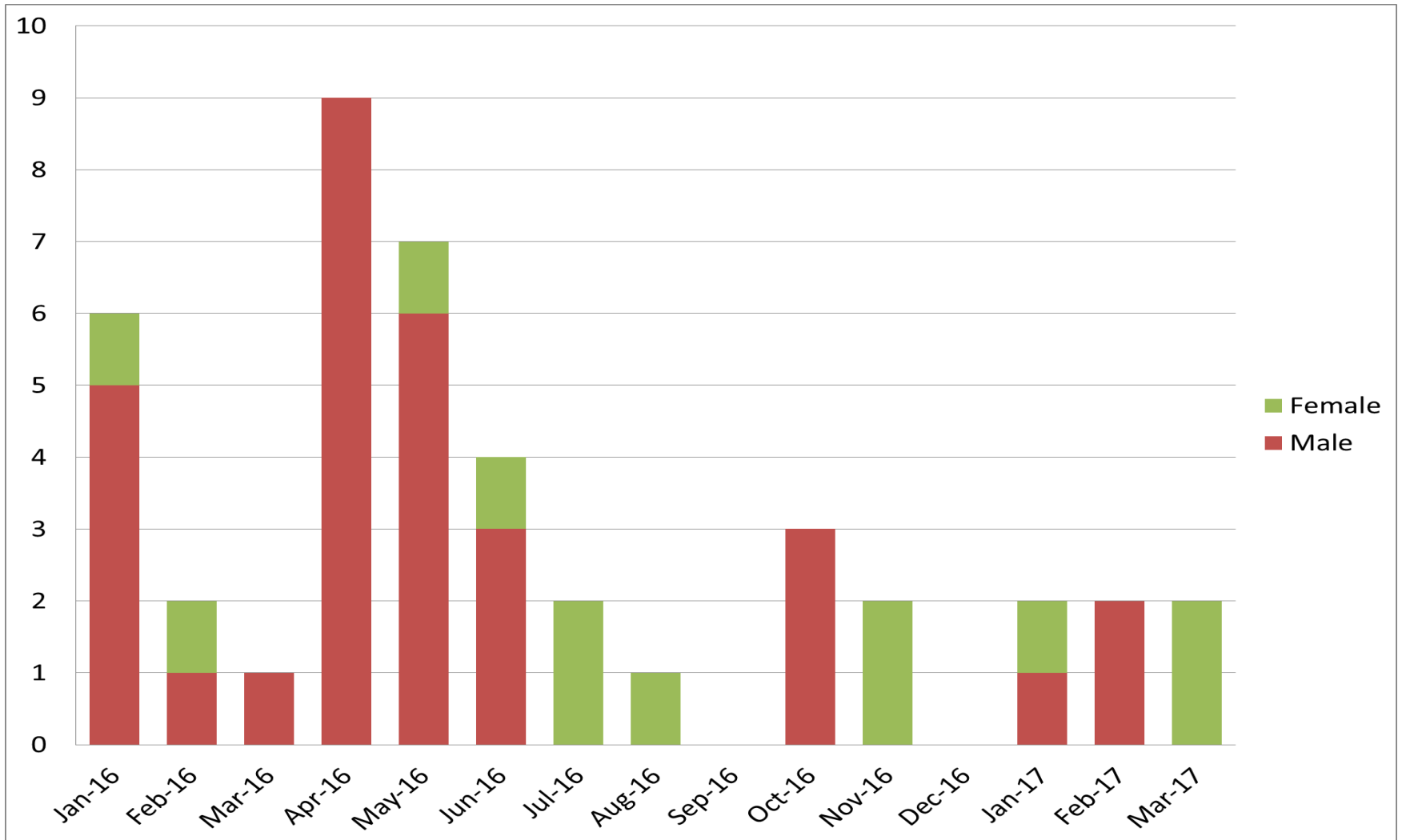
ID-HEV Screening (ver 2)

(4th Jan 2016 – 31st March 2017)

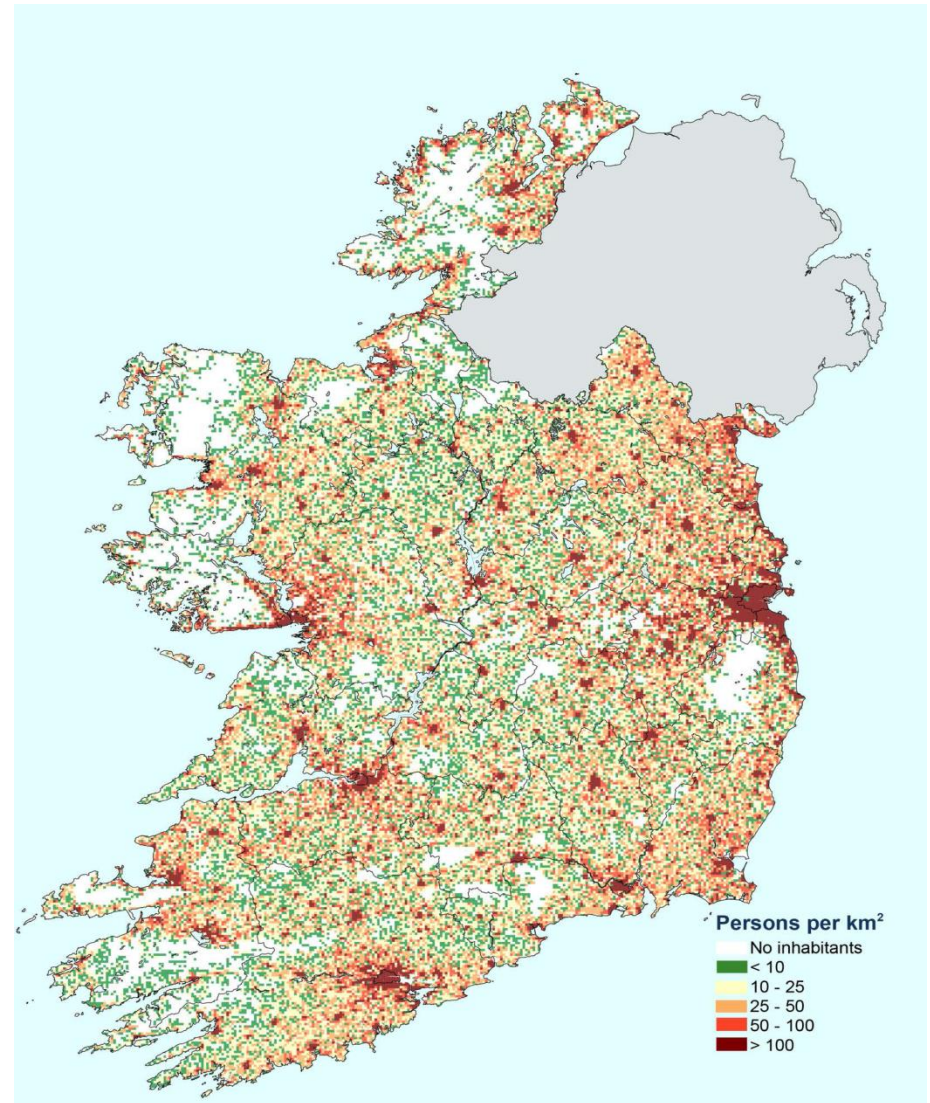


Frequency of HEV Positives

Jan 2016 to March 2017



Geographical Distribution



Universal HEV RNA screening

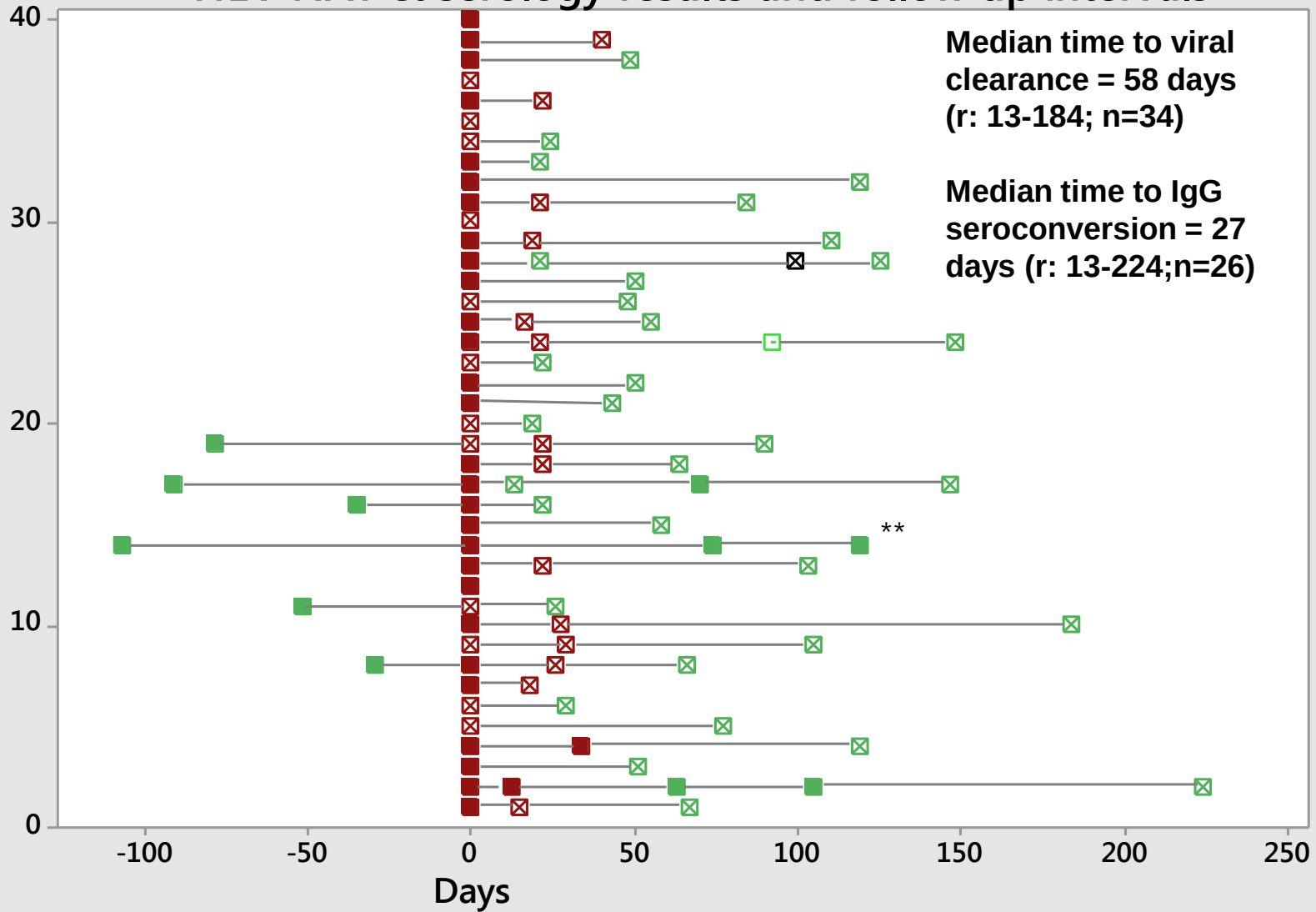
4th Jan 2016 - 31st March 2017

- 43 of 176,918 donations HEV positive: 1:4,114
1 : 1,887 donors (n=81,146)
- M:F 31 vs 12;
- 4 platelet apheresis: 39 WB donors
- Anti-HEV
 - IgM(-)/IgG(-) 26 (65%)
 - IgM(+) IgG(-) 2 (5%)
 - IgM(+) IgG(+) 10 (25%)
 - IgM(-) IgG(+) 2 (5%)

HEV Positive donors

Male			Female		Both		
Age Group	Donors (%)	Positives (%)	Donors (%)	Positives (%)	Donors (%)	Positives (%)	
18 - 29	7,403 (12.6)	6 (0.08)	5,354 (24.0)	7 (0.13)	12,757 (15.7)	13 (0.1)	Age group:
30 - 39	11,984 (20.4)	8 (0.07)	5,186 (23.2)	3 (0.06)	17,170 (21.1)	11 (0.06)	18-49 v
40 - 49	16,206 (27.6)	11 (0.07)	5,589 (25.0)	1 (0.02)	21,795 (26.9)	12 (0.06)	50+
50 - 59	16,763 (28.5)	5 (0.03)	5,989 (26.8)	1 (0.02)	22,752 (28.0)	6 (0.03)	p <0.005
60yrs	6,458 (11.0)	1 (0.01)	214 (0.96)	0	6,672 (8.2)	1 (0.01)	Chi- sq
Totals	58,812	31 (0.05)	22,332	12 (0.05)	81,146	43 (0.05%)	
Male v Female p = 0.955							

HEV NAT & serology results and follow up intervals

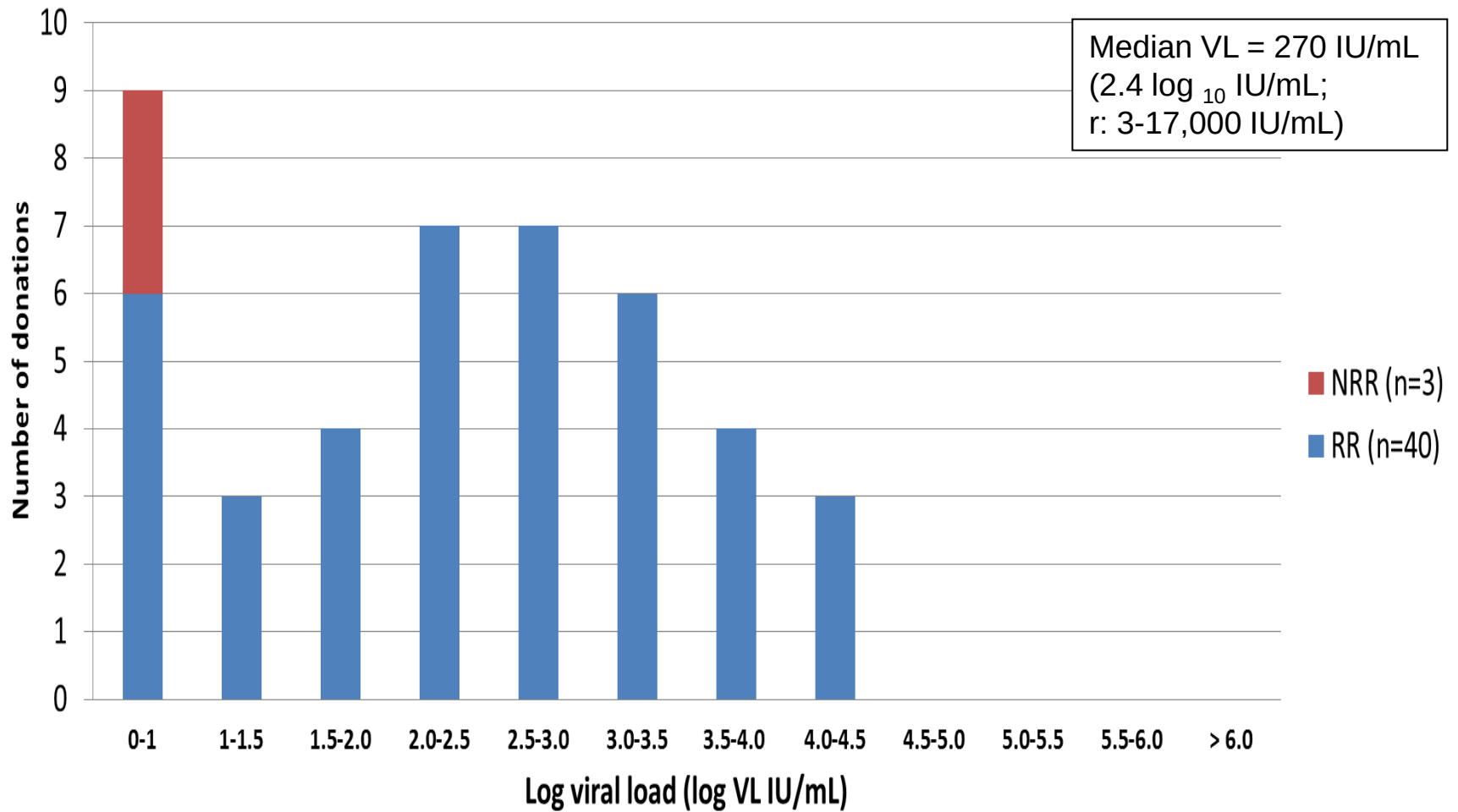


Median time to viral clearance = 58 days (r: 13-184; n=34)

**Median time to IgG
seroconversion = 27
days (r: 13-224;n=26)**

■ NAT +  Sero +
■ NAT -  Sero -

Distribution of HEV RNA Viral Load



HEV Genotyping

PHE: ORF1

G3 efg = 3 Clade 1

G3 abchij = 3 Clade 2

One outlier

SANQUIN:

Subtype	ORF1	ORF2	Clade
3a	1	1	2
3c	10	9	2
3e	9	4	1
3f	2	1	1
3 outlier	3	1	?
Total	25	16	

Of a total of 31 : 14 Clade 1 and 14 Clade 2 and 3 outliers

non seroconverters

1) Outlier

RR S/Co 36.36 ,PCR + x2 Serology neg, viral load 893 IU/mL

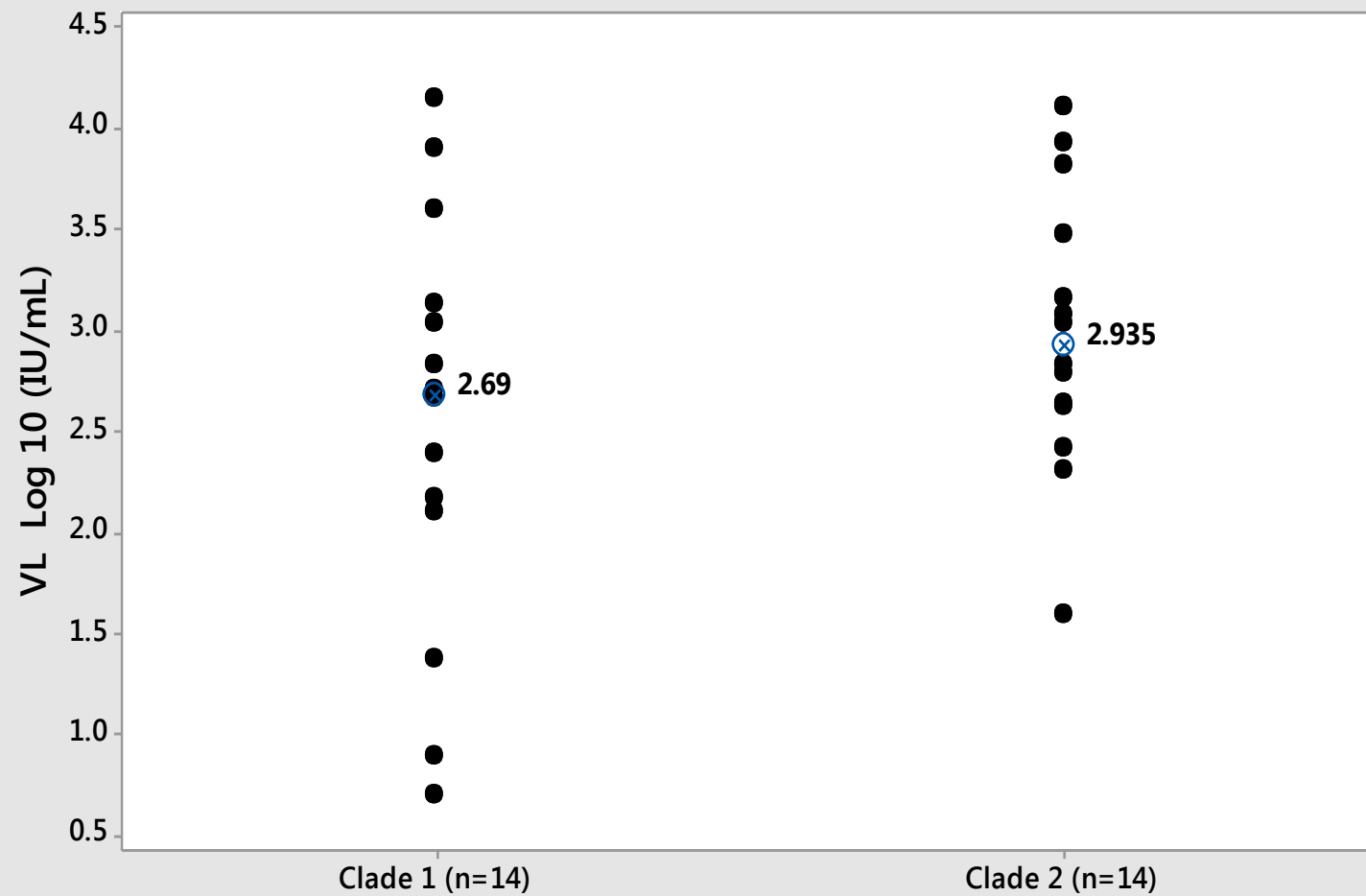
F/U 12 days HEV RNA +(S/Co 4.9) PCR –	IgM Neg (0.875); IgG Neg (0.216)
F/U 63 days HEV RNA Neg	IgM Neg (0.621); IgG Neg (0.142)
F/U 105 days HEV RNA Neg	IgM Neg (0.299); IgG Neg (0.521)
F/U 224 days HEV RNA Neg	IgM Neg (0.03); IgG Pos (1.889)

2)

IR S/Co 1.43-5/11 replicates pos, PCR pos x1, serology neg

F/U at 74 days HEV RNA Neg	IgM Neg (0.167); IgG Neg (0.074)
F/U at 119 days HEV RNA Neg	IgM Neg (0.075); IgG Neg (0.095)
PHE viral load <100 IU/mL	Sanquin 8 IU/mL
3e sequence identical to a confirmed pos tested 5 days later	

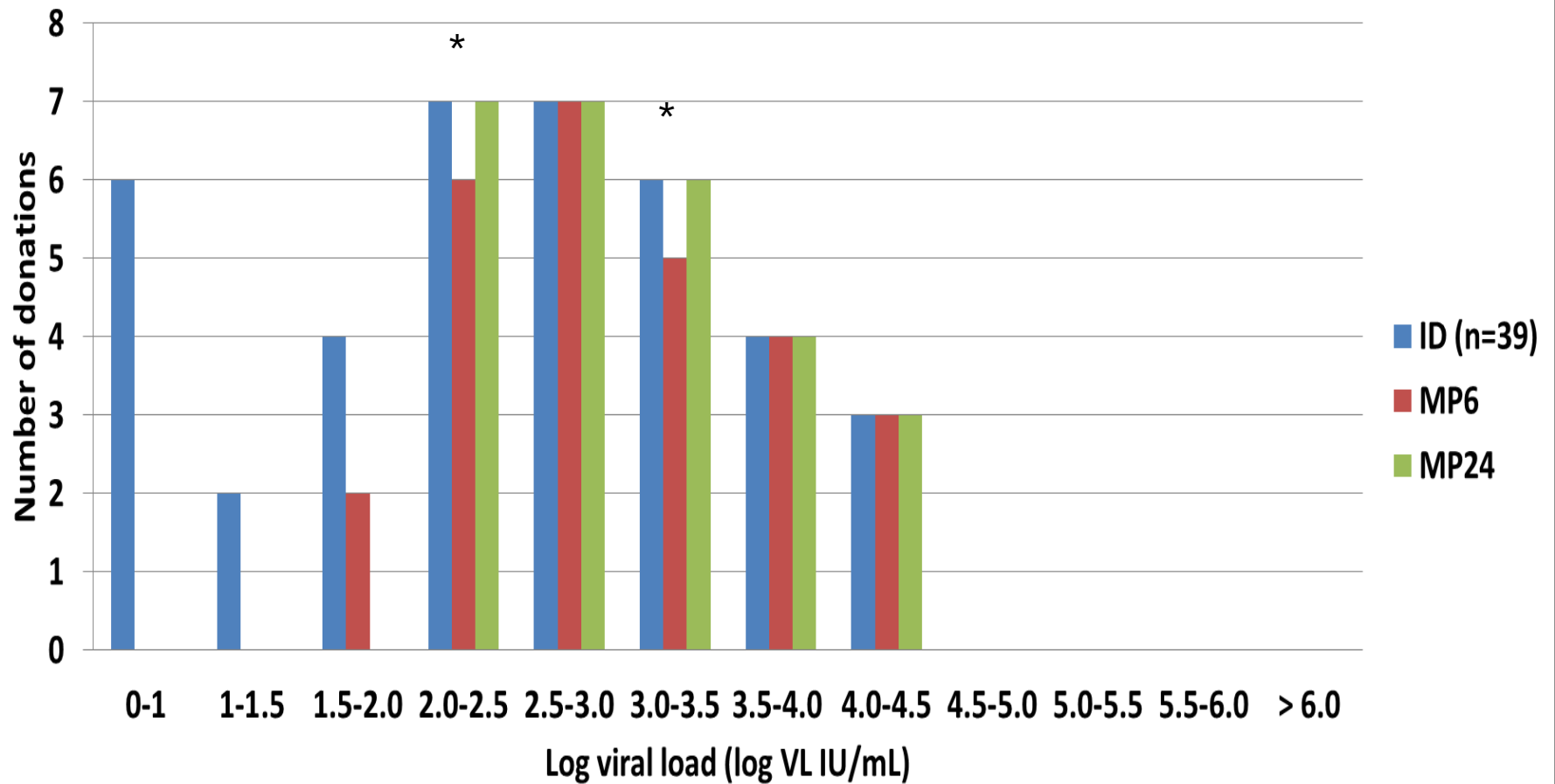
Viral Load: Clade 1 v Clade 2



Mann Whitney p=0.29

ID-NAT v MP-6 v MP-24

Distribution of HEV Viral Loads



* 2/3 replicates Reactive

Donor Interviews (n= 38)

- Median time 24 days (r 12-121)
- 36 Irish
- 11 (29%) some symptomatology
Fatigue 7/11 (64%) usually pre donation
- 3 (8%) –more significant
- G3 –Clade 1: 5 of 14 (35.7%) symptomatic vs
Clade 2 : 3 of 12 (25%) $p=0.55$ Chi sq.

Food Questionnaire (n=38)

- No vegetarians
- Chicken 97%
- Bacon 84%
- Pork sausages 84%
- Ham 79%
- Pork 76%
- Cured pork meat 74%
- Black pudding 61%
- Shellfish 53%
- Pate 21%
- Game 11%
- Pork pie 5%
- No occupational exposure (1 farmer 2 lived on farms dairy no pigs)
- Travel 9/38 (24%), USA 3, Europe 3, UK 2



Conclusions

- HEV RNA prevalence is 1:4114 donations
2016: 1:2447 to 1:8844
- Sig ass younger donors (<50 yr)
- Medium time to viral clearance 8 weeks
- low viral loads median 270 (r 3 -1700) IU/mL
- 28 G3 ; 50%: 50%, Clade 1 vs Clade 2,
- Three G3 outliers
- MP-24 missed 12/39 (31%) of ID-NAT +, all <100 IU/mL
- No vegetarians, 71% asymptomatic
- 2016 HEV notifiable disease in Ireland (90 HEV, 38 HAV)

With Thanks

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