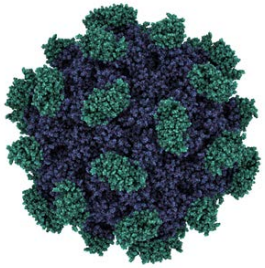
NHS
Blood and Transplant



Hepatitis E Virus in Transfusion and Transplantation - The Story so far

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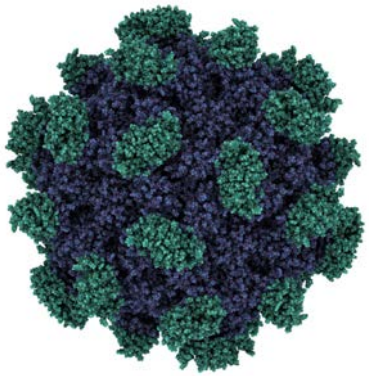
Disclosures

Grifols sponsored speaker ISBT 2014



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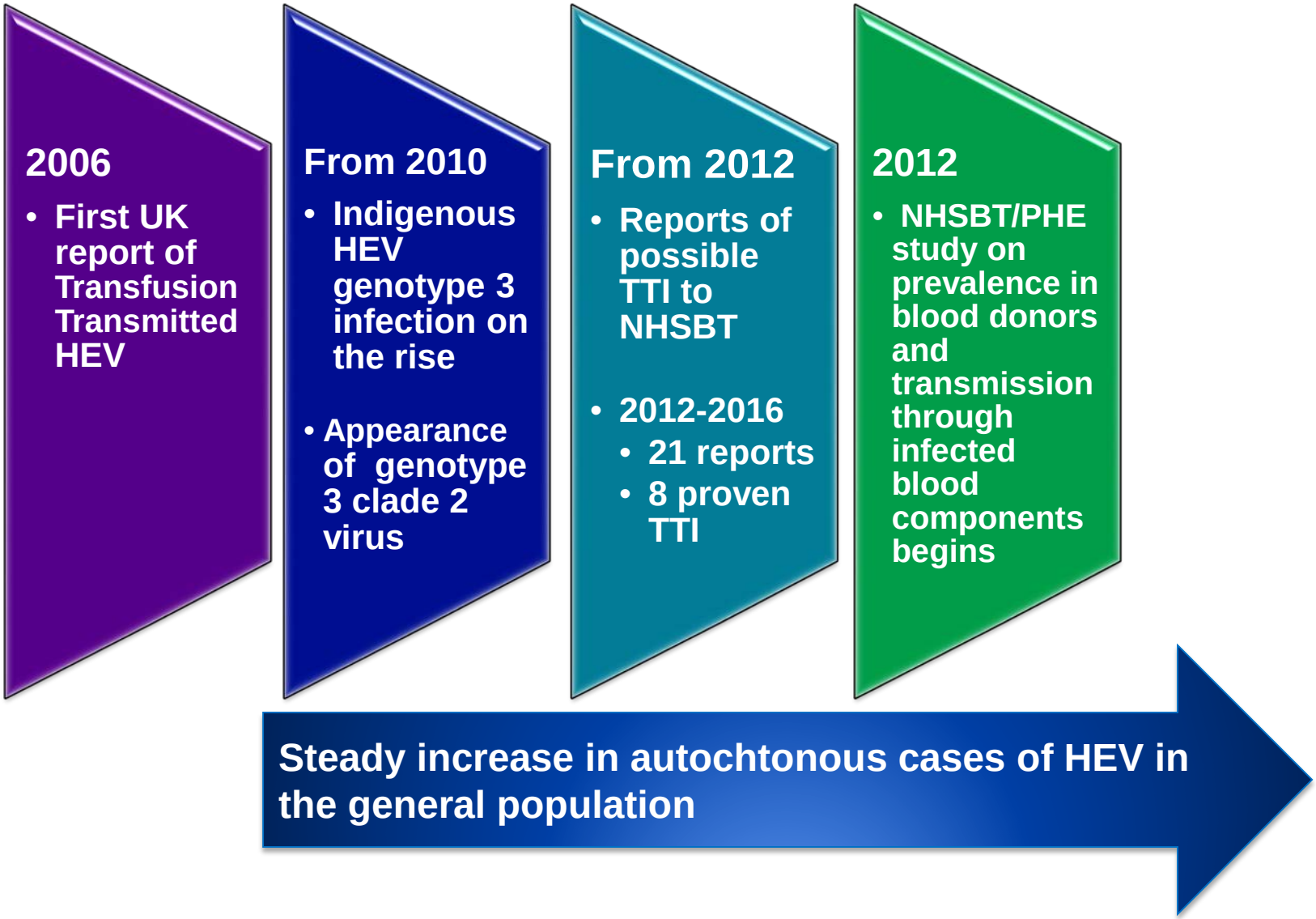
Public Health England

NHS Blood and Transplant

Hepatitis E Virus (HEV) – UK Timeline-



HEV – UK Timeline

NHS Blood and Transplant

2012

- Reports of potential TTI cases to NHSBT begin to increase
- NHSBT/PHE HEV Prevalence and Transmission Study begins

2014

- NHSBT/PHE HEV Prevalence and Transmission Study is published
- **SABTO 1st HEV Working Group**

2015

- **SABTO Guidance** – Screened components for stem cells and solid organ transplant recipients
- Increase in awareness and in HEV case ascertainment (immunocompromised patients)

2016

- **NHSBT introduces partial blood donor screening (HEV NAT pool 24)**
  - 27% donors tested to meet demand
  - 0.04% confirmed positivity rate
- **SABTO 2nd HEV Working Group**
- **SaBTO Recommendation - Universal HEV RNA screening of donors (blood, stem cells, tissues and organs)**

2017

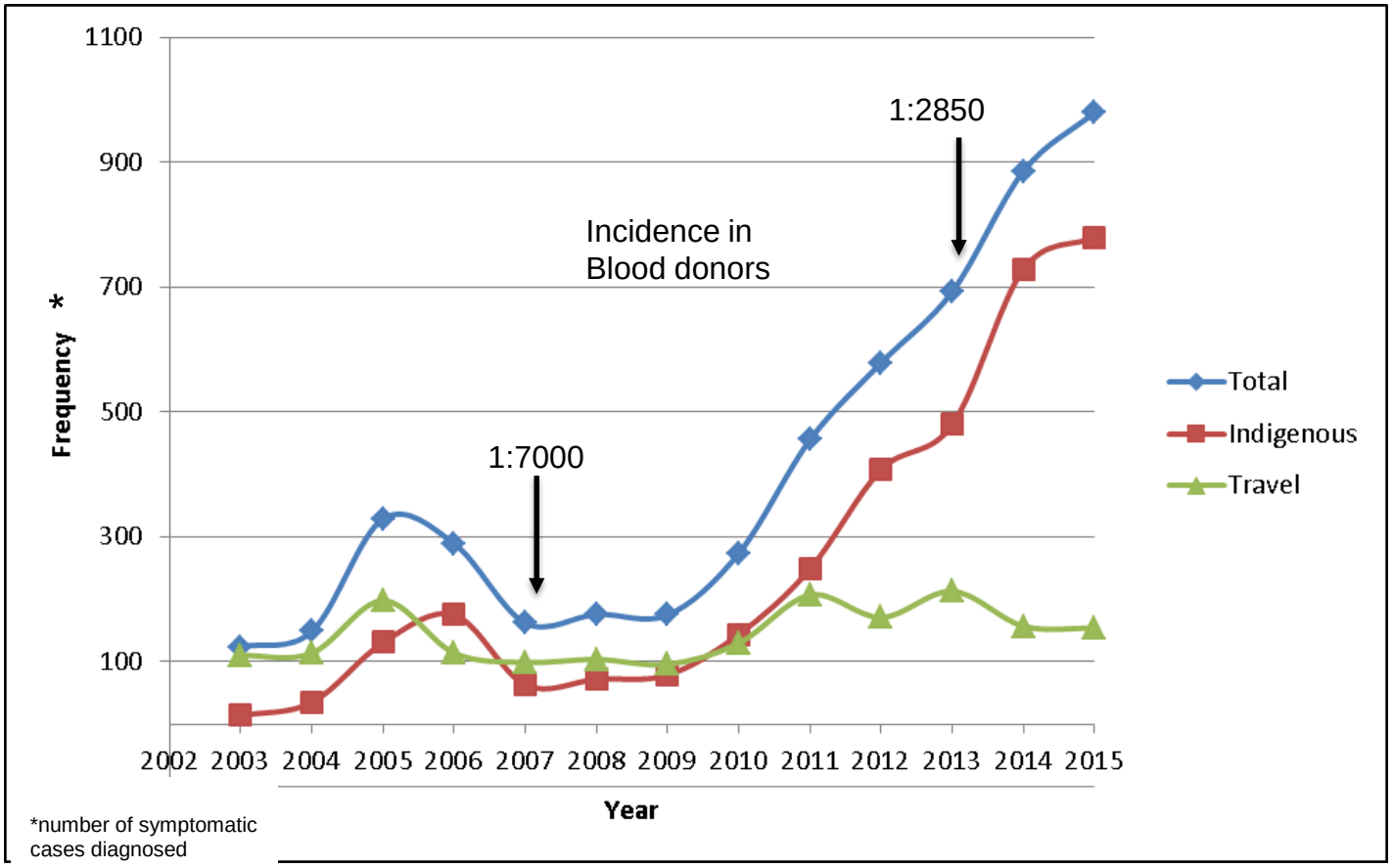
- **NHSBT introduces universal screening of blood donors**
- HEV NAT screening of NHSBT stem cell, tissue and organ donors to be implemented in Autumn

Public Health England

NHS Blood and Transplant

Enhanced Surveillance of HEV infection in England & Wales

Public Health England (PHE) has been running a programme of enhanced surveillance in the general population since 2003



Public Health England

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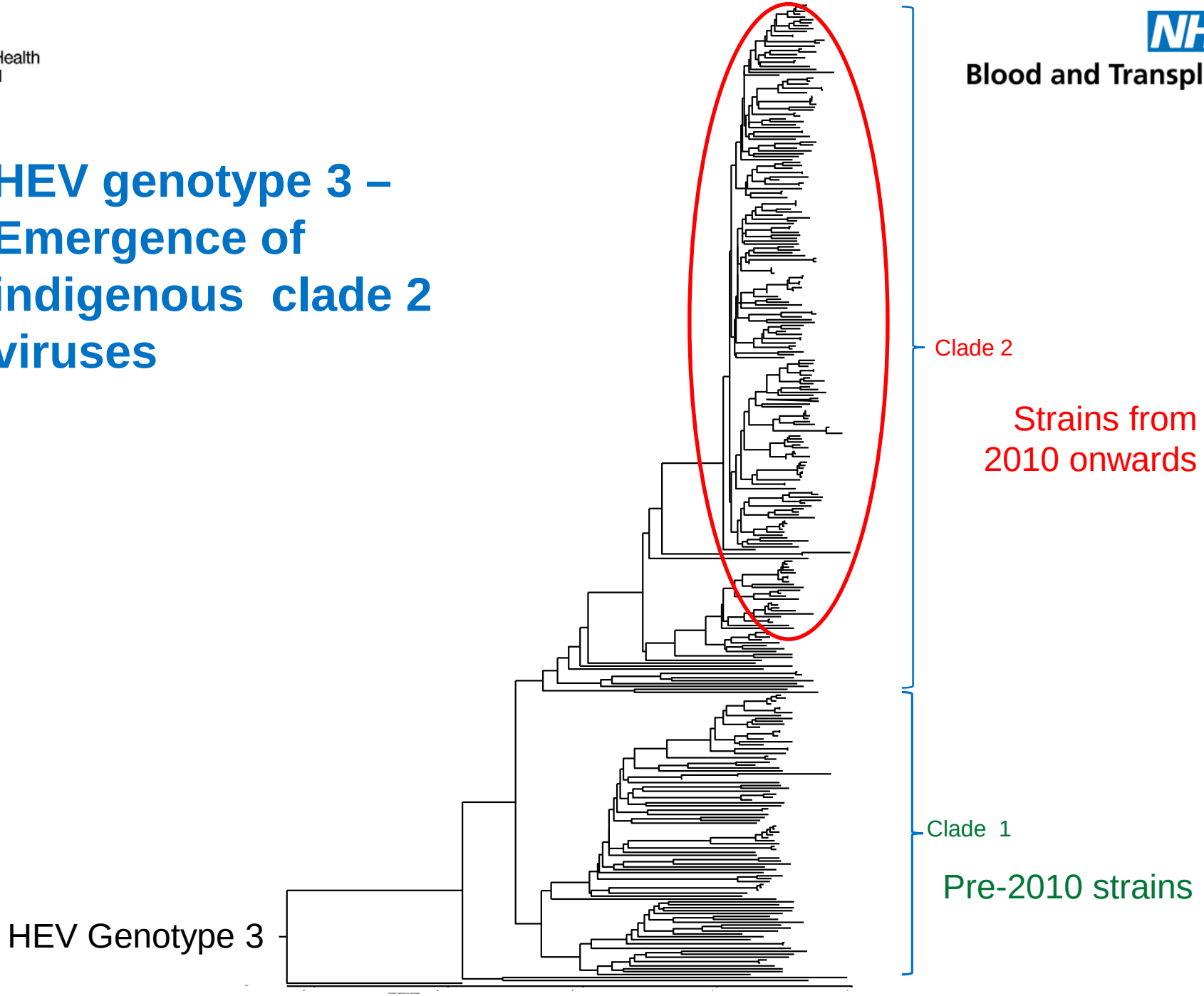
HEV genotype 3 – Emergence of indigenous clade 2 viruses



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Impact and Outcome of Hepatitis E Virus Infection

Persistent Infection

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Transfusion-Transmitted HEV

Case studies

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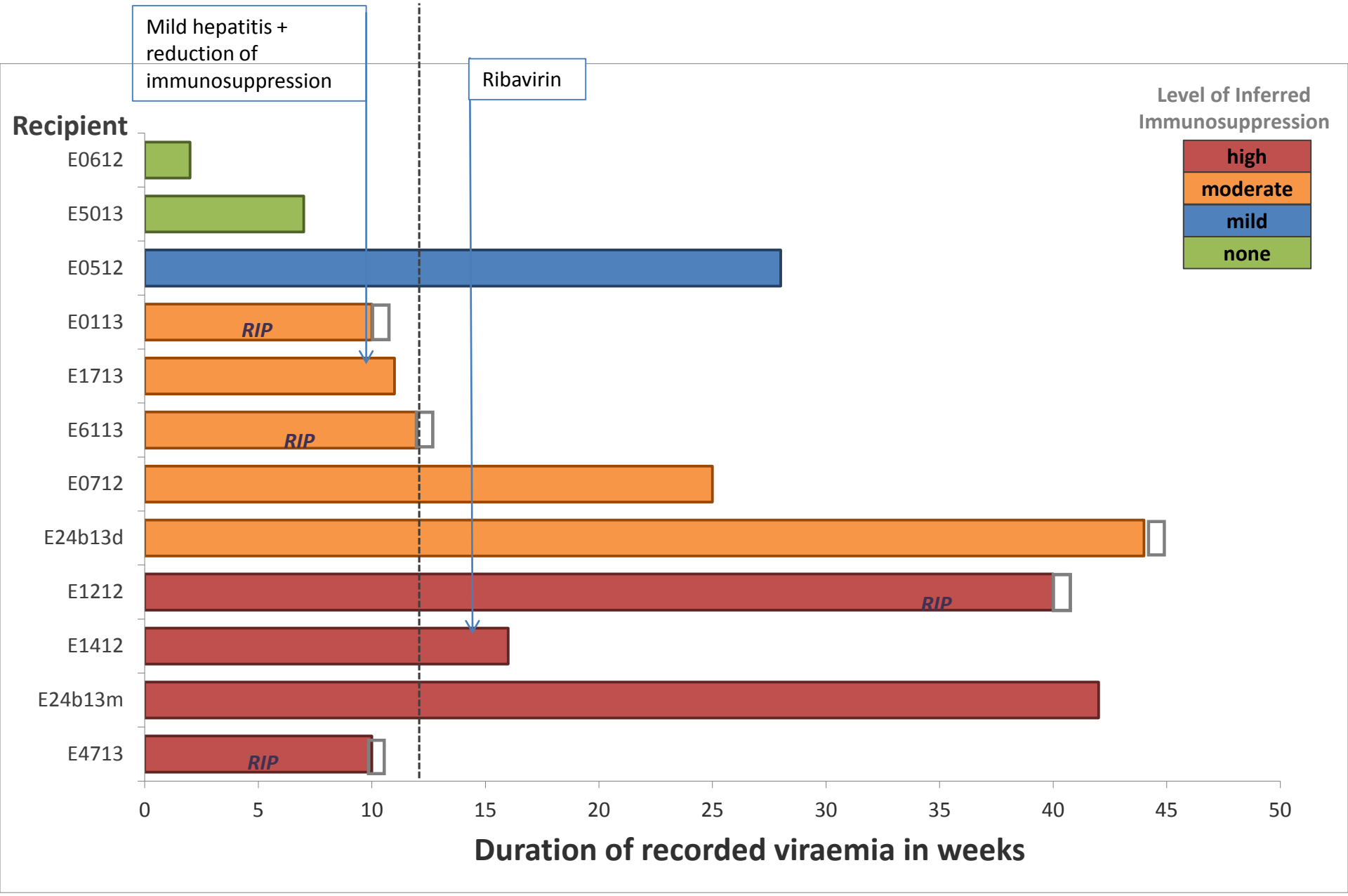
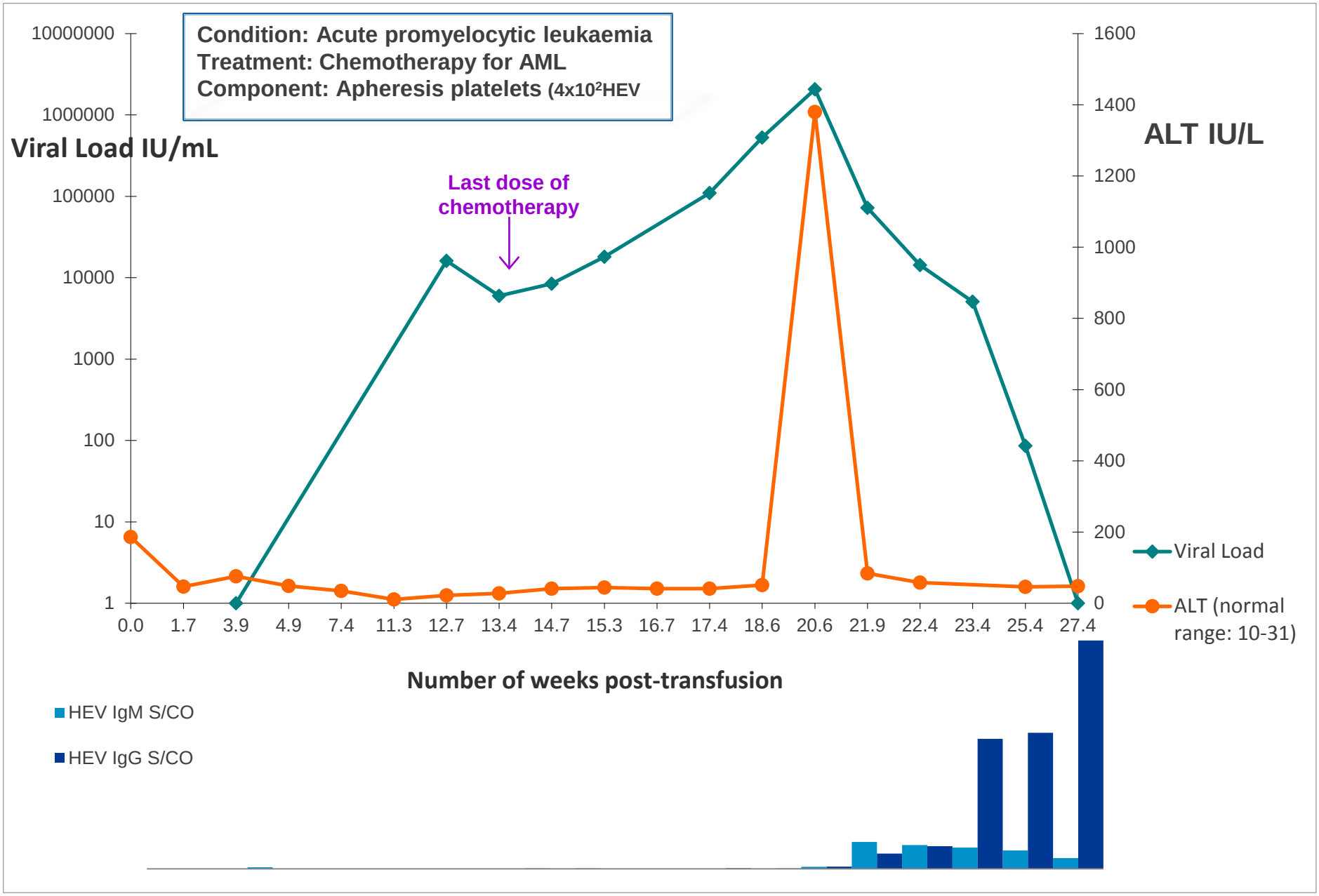
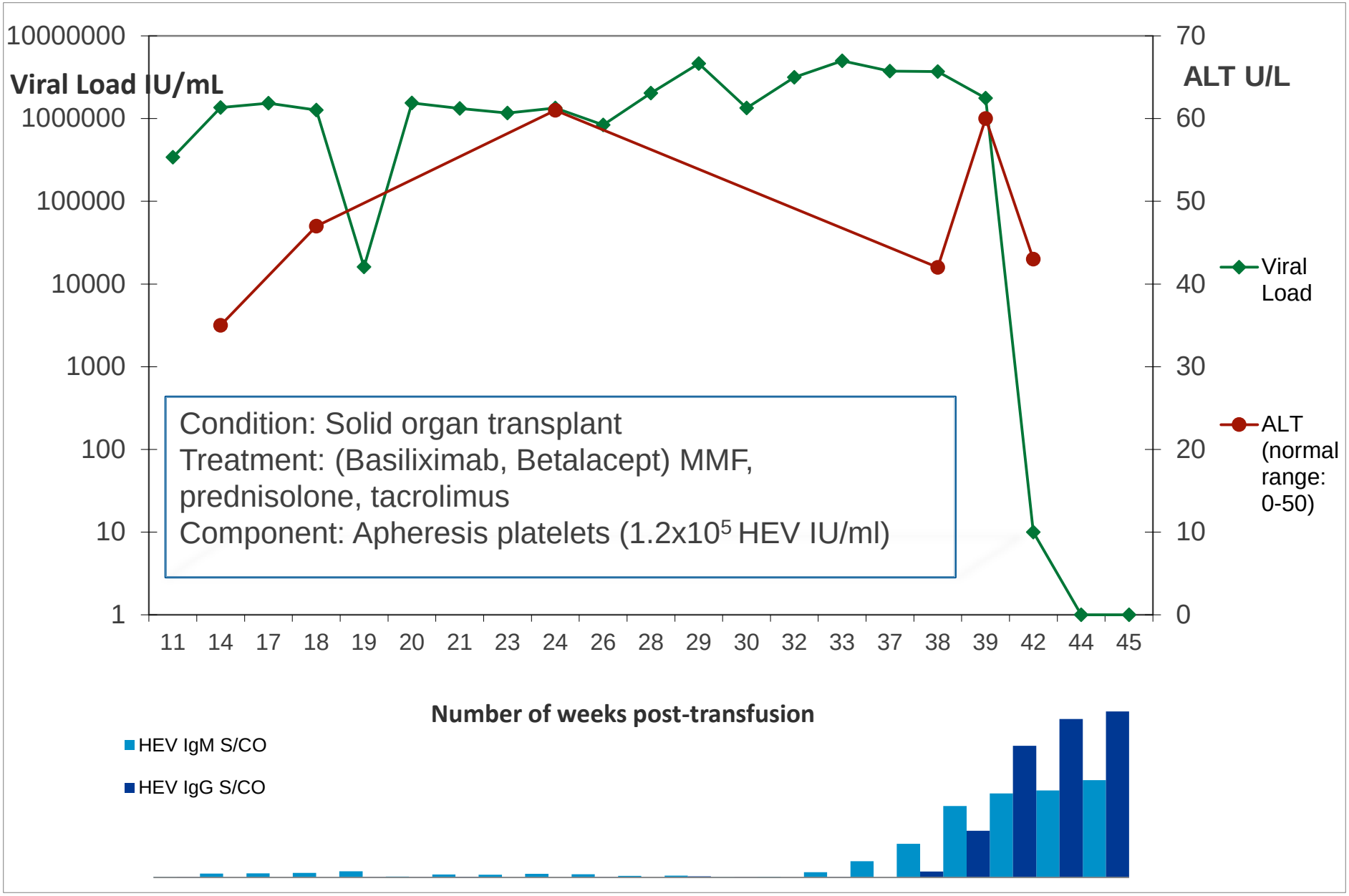
Outcome of HEV infection in viraemic recipients



Moderately Immunosuppressed Recipient



Significantly immunosuppressed recipient
Prolonged viraemia, with control



NHS Blood and Transplant

Transfusion-associated HEV transmission

- First UK transfusion-transmitted infection reported in 2006
- 21 cases of possible TTI reported for investigation between 2012 and 2016
- 8 proven transfusion-transmitted events

Recipient Underlying Diagnosis	Donor Exposures	Implicated Component
Allogeneic stem cell transplant *	33	Fresh frozen plasma
Vasculitis, renal failure *	129	Fresh frozen plasma
Alcoholic liver disease	17	Fresh frozen plasma
Rectal carcinoma *	17	Red blood cells
Autologous stem cell transplant *	33	Pooled platelets & apheresis platelets
Liver transplant recipient *	33	Apheresis platelets
Non-Hodgkin's lymphoma	18	Cryoprecipitate
Aplastic anaemia	10	Red blood cells

same donor exposure

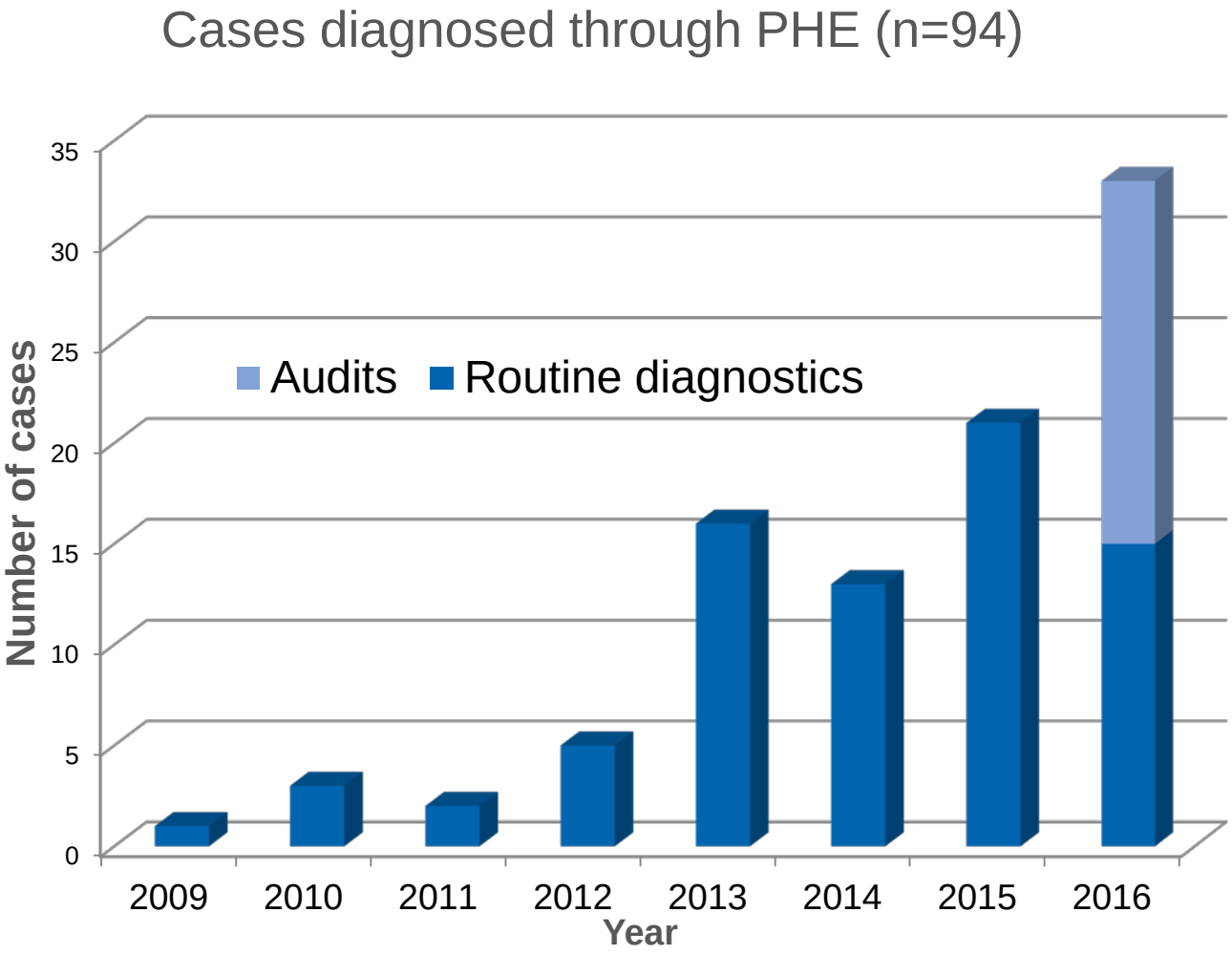
same donor exposure

**** persistent infection 5/8***

Public Health England

NHS Blood and Transplant

Persistent HEV in England & Wales 2009-2016 (1)



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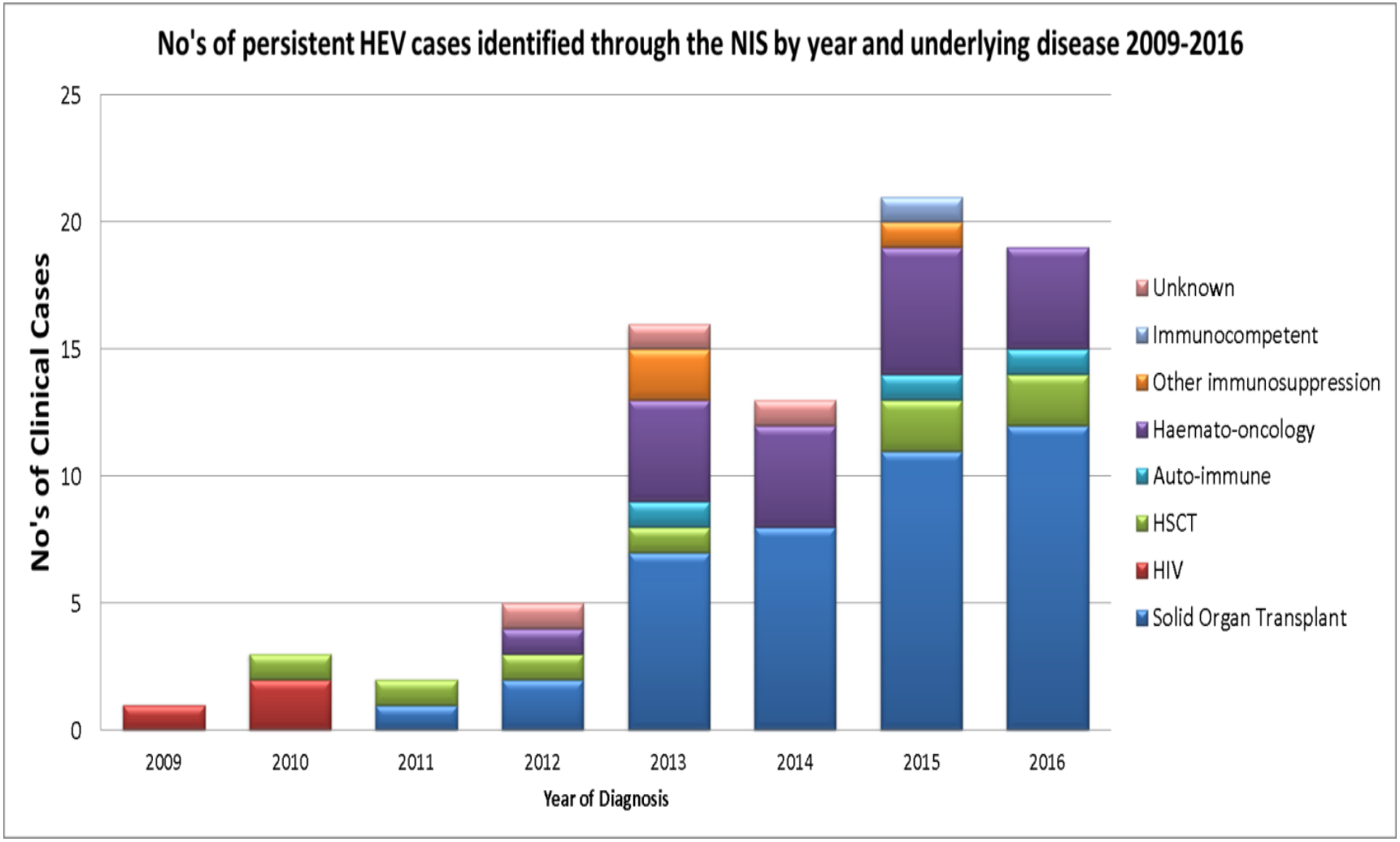
NHS Blood and Transplant

Persistent HEV in England & Wales 2009-2016 (2)



Public Health England

NHS Blood and Transplant

Persistent HEV infections – underlying conditions other than transplantation

Other category	No	Drug regimens
Rheumatoid Arthritis	1	Methotrexate, Prednisolone
Waldenstrom macroglobulinaemia	1	Bendamustine; Rituximab
anti-GBM glomerulonephritis	1	Cyclophosphamide
Neurosarcoidosis	1	Methotrexate, Prednisolone
Aplastic anaemia	2	Unknown
Inflammatory Bowel Disease	1	Azathioprine
Not known to be immunosuppressed	1	n/a

SaBTO

Advisory Committee on the Safety of Blood, Tissues and Organs

- 2015 recommendations: Implementation of selective HEV RNA screening for blood donors
- Blood components destined for solid organ and stem cell transplant recipients
  - Patients awaiting solid organ transplant (SOT) – from 3 months prior to date of planned elective SOT or from the date of listing
  - Patients who have had SOT –whilst on immunosuppressants
  - Patients with acute leukaemia – from diagnosis and whilst awaiting for a stem cell transplant
  - Patients awaiting allogeneic stem cell transplant – from 3 months prior to the date of planned transplant and up to 6 months following transplant, or for as long as the patient is immuno-suppressed

2nd SaBTO HEV Working Group (2016)

- Undertake an assessment of the cost-effectiveness of different strategies to reduce the risk of HEV acquisition through blood, cells, tissues and organs
- Review several issues, including:
  - feedback received from a range of stakeholders on operational practices
  - clinical recommendations on the use of HEV screened components
  - evidence for HEV transmission via transplanted organs, stem cells and tissues

NHS Blood and Transplant

Which patients need to be protected from HEV infection? (1)

- Evidence that immunocompromised patients outside the solid transplant setting are also at risk from acute and persistent HEV infection
  - Patients with evidence of severe primary immunodeficiency
  - Patients currently being treated for malignant disease with immunosuppressive chemotherapy or radiotherapy, or who have terminated such treatment within at least the last 6 months
  - Patients receiving systemic high dose steroids until at least 3 months after treatment has stopped

NHS
Blood and Transplant

Screening of donors of SoHO

- The evidence of transmission through transplantation of solid organs, tissues and haematopoietic stem cells remains minimal
- There must be an assessment of the risk of infection and the clinical consequence of transmission
- The consequence of a transmission could justify screening donor
- The small, but identifiable, clinical benefit of screening donors of organs, tissues and stem cell maintains consistency of approach in protecting highly vulnerable patients from HEV infection

SaBTO

Advisory Committee on the Safety of Blood, Tissues and Organs

Recommendations from the expert advisory committee on the Safety of Blood, Tissues and Organs (SaBTO) on measures to protect patients from acquiring hepatitis E virus via transfusion or transplantation

These recommendations were approved by SaBTO on 1 Nov 2016.

Universal screening

NHS Blood and Transplant

Blood donors

- Started on 15th April 2017 (NHSBT)
- Screening undertaken in pools of 24
- Confirmation of screen positives by NHSBT reference laboratory using an alternative assay

Non-blood donors

- Strategy for stem cells and tissue donors will vary
- Organ donors to be screened individually
- HEV RNA positivity not an absolute contra-indication for donation
- HEV RNA status of deceased organ donors will be determined after donation

NHSBT HEV RNA blood donor testing February 2016 to July 2017

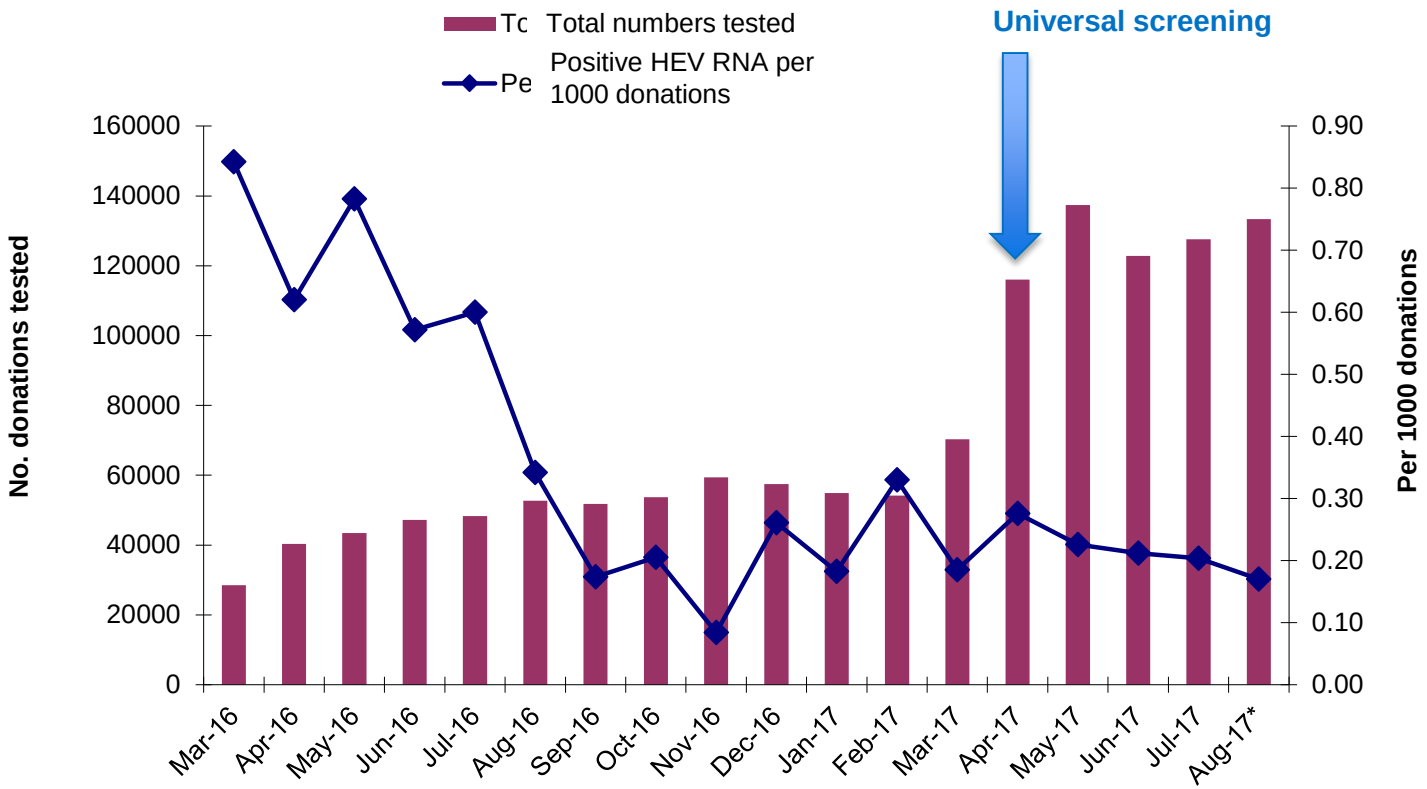
NHS Blood and Transplant

Month 2016/17	Donations tested	Confirmed RNA positive	Prevalence rate	% of donations positive
February	603	1	1 in 603	0.17
March	28491	24	1 in 1187	0.08
April	40305	25	1 in 1612	0.06
May	43443	34	1 in 1277	0.08
June	47232	27	1 in 1749	0.06
July	48329	29	1 in 1666	0.06
August	52672	18	1 in 2926	0.03
September	51784	9	1 in 5753	0.02
October	53668	11	1 in 4878	0.02
November	59362	5	1 in 11872	0.01
December	57472	15	1 in 3831	0.03
January	54866	10	1 in 5486	0.02
February	54183	18	1 in 3010	0.03
March	70303	13	1 in 5408	0.02
Universal screening ⇨ April	116066	32	1 in 3627	0.03
May	137372	31	1 in 4431	0.02
June	122775	26	1 in 4722	0.02
July	127577	26	1 in 4907	0.02
TOTAL	**1166503**	**354**	**1 in 3295**	**0.03**

Public Health England

NHS Blood and Transplant

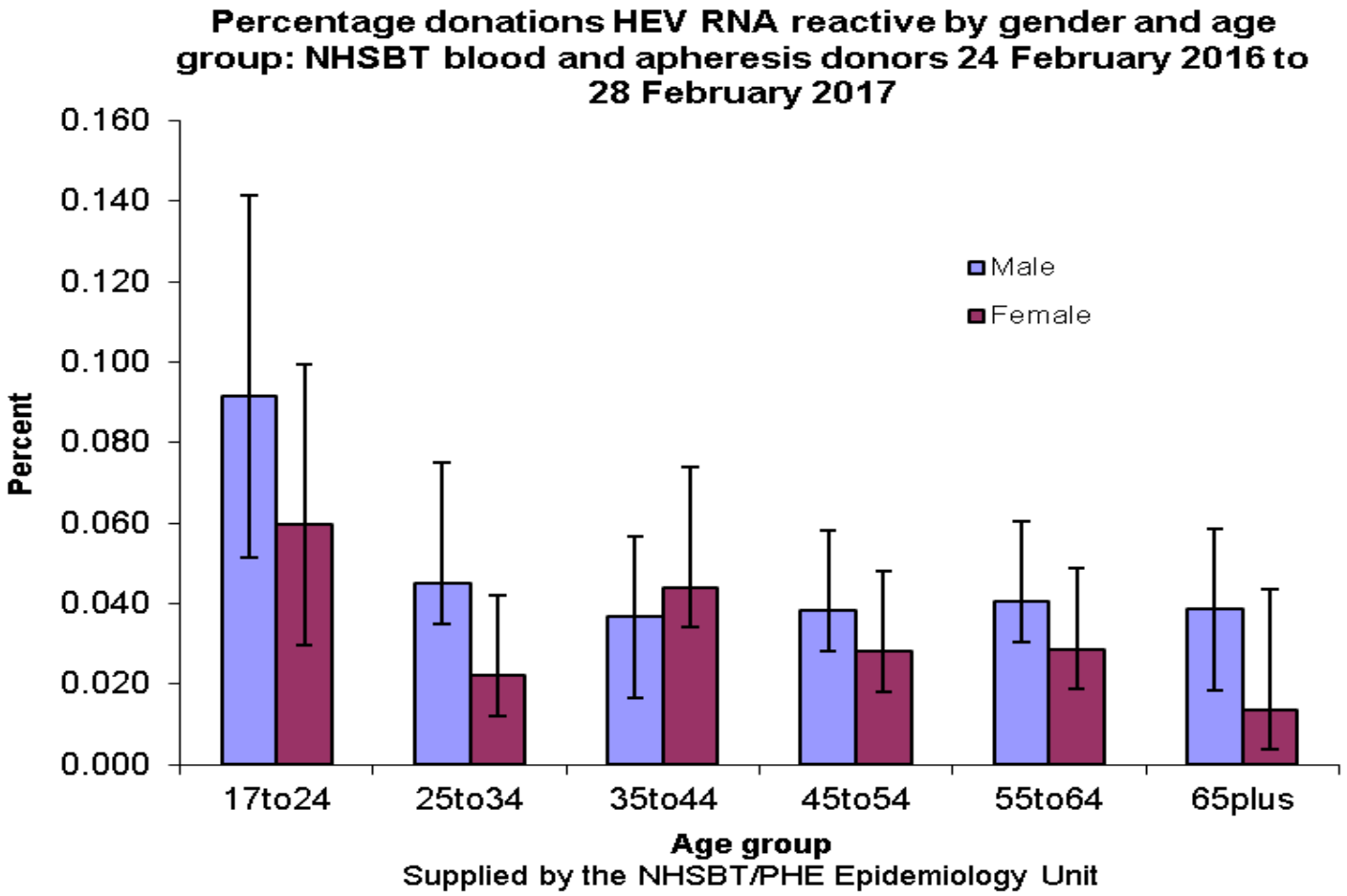
NHSBT HEV RNA blood donor testing February 2016 to August 2017



Data supplied by the NHSBT/PHE Epidemiology Unit

Public Health England

Donor demographics: Gender and age



Conclusion

NHS Blood and Transplant

- Continuing acquisition of knowledge on HEV will inform future guidance and policies on the safety of SoHO
- Report on the impact of UK guidance will be produced in Autumn 2017 and yearly thereafter (blood services + public health bodies)
- Recommendation will be reviewed in 3 years
- **Education and information**:The dietary route is the main source of infection, so it is important to reinforce the need to cook pork and pork-derived food well
- **Increased awareness** about HEV infection and its impact on immunosuppressed patients should lead to more testing, monitoring and better management in order to avoid complications of persistent infection

Acknowledgments

- Donors, patients, and their carers
- NHSBT
  - Microbiology services
    - Clinical team
    - Surveillance Team
    - National Transfusion Microbiology Reference laboratory
- Public Health England
  - Blood Borne Virus Unit
  - NHSBT/PHE joint Epidemiology team
  - Surveillance Unit

NHS
Blood and Transplant

Thank you

Yes I donate
ORGAN DONATION

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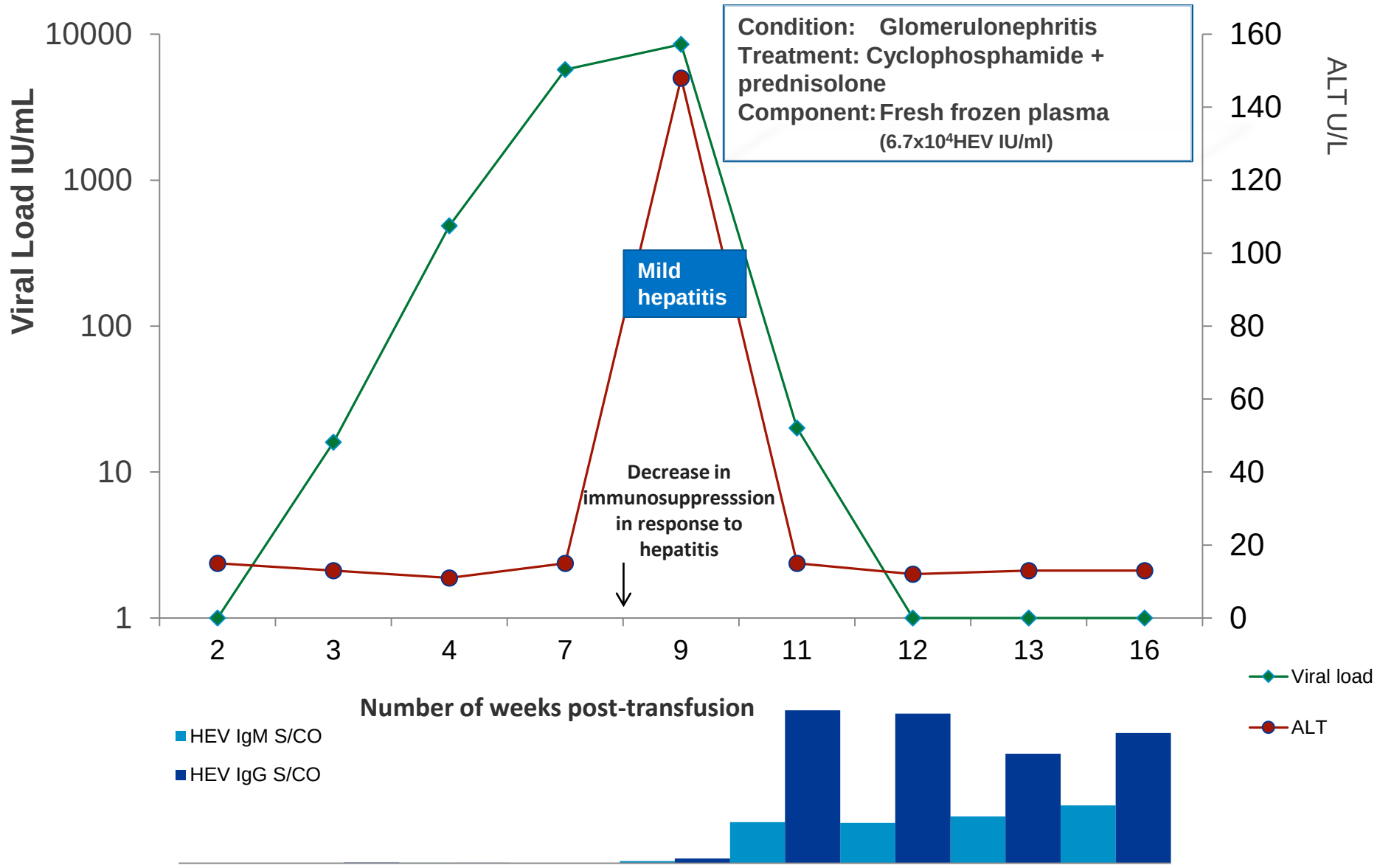
Blood and Transplant

Slide holder

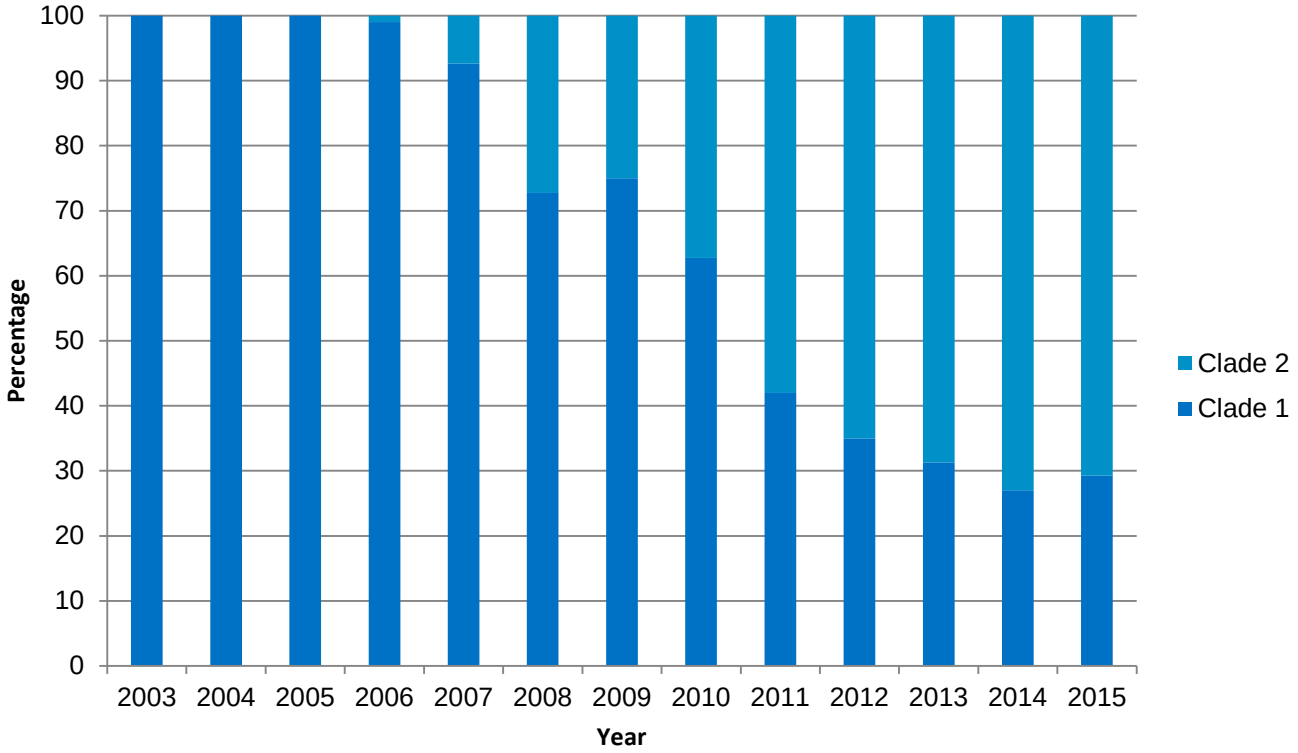
Symptomatic clearance of HEV



Public Health England

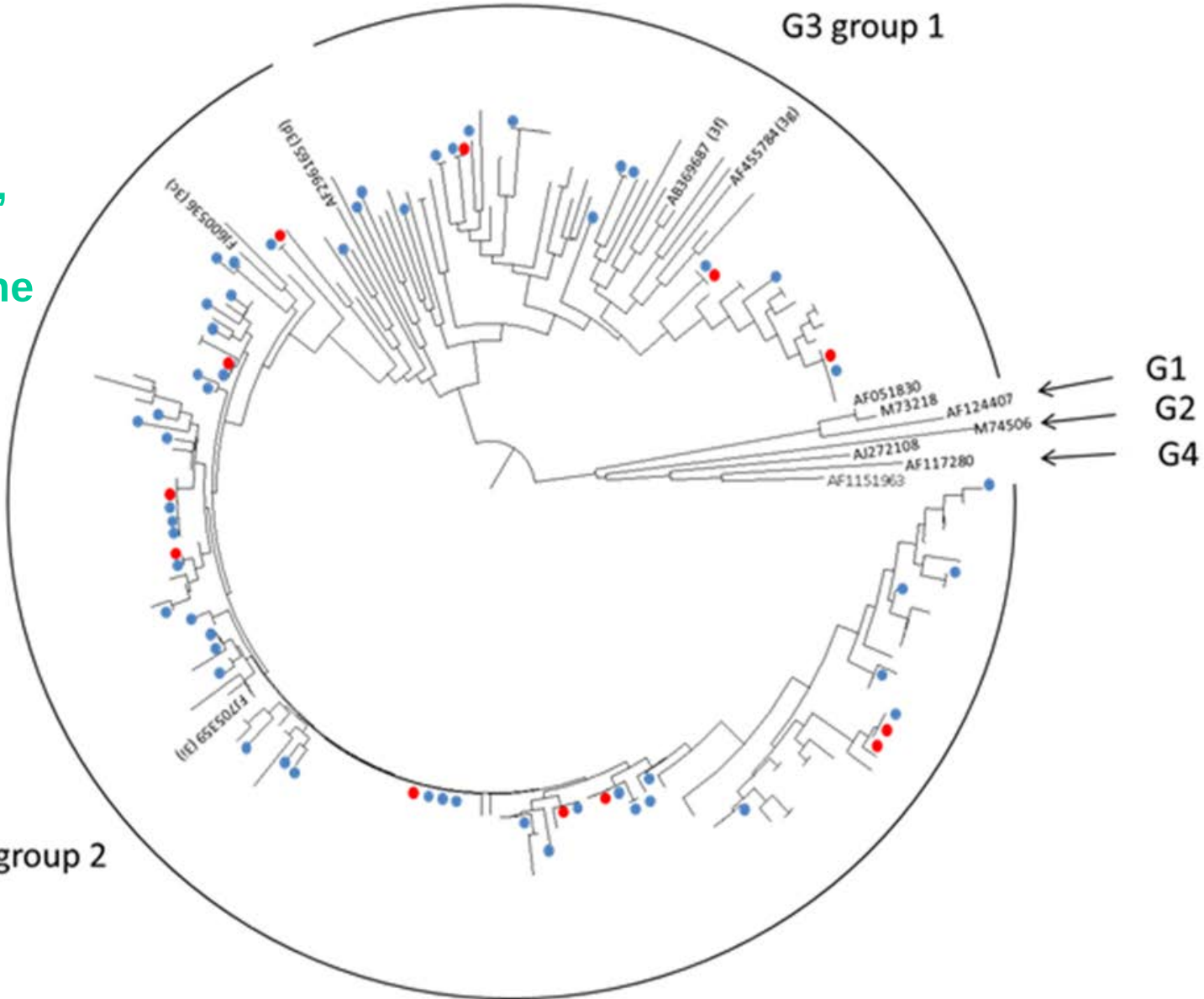
NHS Blood and Transplant

Proportion of HEV Genotype 3 clade 1 and 2 sequences - 2003-2015



- Increased awareness of HEV infection
- Increased recognition of chronic HEV infections in the immunosuppressed population
- Prevalence of persistent infection in the various increased risk groups is not known
- Collate data on these cases, including demographics, clinical details, virological markers, treatment and outcomes
- Understanding of the determinants of persistence, triggers for treatment and outcomes

Phylogenetic analysis of community acquired HEV , donors and recipients in the HEV study



Hepatitis E virus in blood components: a prevalence and transmission study in southeast England

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Katherine Russell, Kate I Tettmar, Joanne Tossell, Ines Ushiro-Lumb, Richard S Tedder

Lancet 2014; 384: 1766–73
Published Online
July 28, 2014

Summary

Background The prevalence of hepatitis E virus (HEV) genotype 3 infections in the English population (incl
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http://dx.doi.org/10.1016/S0140-6736(14)61034-5
See Comment page 1729

Transfusion Microbiology,

Summary

Background The prevalence of hepatitis E virus (HEV) genotype 3 infections in the English population (including blood donors) is unknown, but is probably widespread, and the virus has been detected in pooled plasma products. HEV-infected donors have been retrospectively identified through investigation of reported cases of possible transfusion-transmitted hepatitis E. The frequency of HEV transmission by transfusion and its outcome remains unknown. We report the prevalence of HEV RNA in blood donations, the transmission of the virus through a range of blood components, and describe the resulting morbidity in the recipients.

- High proportion of blood components given as haematological support to the immunosuppressed population
- Joint NHSBT/PHE study established to look at blood safety
- 225,000 donations screened in 2012/13 for HEV RNA
- Prevalence of 1 in 2850 donations (0.04%)
- 42% transmission rate (related to dose)

Symptoms reported by donors

	Number	Percent
Number of donors reporting symptoms	62	**46**
Fatigue	50	81
Joint pain / aches	15	24
Dark urine	11	18
Feeling ill	9	15
Nausea	8	13
Fever	6	10
Change in appetite	4	6
Stools, pale or loose	4	6
Abdominal pain	3	5
Vomit	2	3
Jaundice	1	2
Neurological	0	0
	97	
Timing recorded for each symptom		
Before donation	21	**22**
Around donation	29	**30**
After donation	47	**48**

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Yes I donate
ORGAN DONATION

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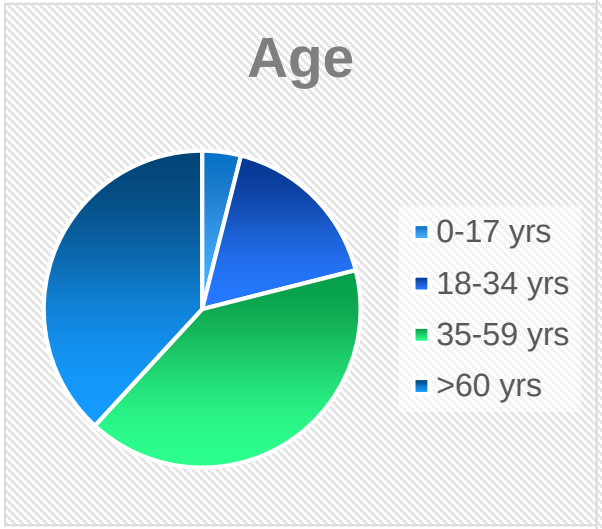
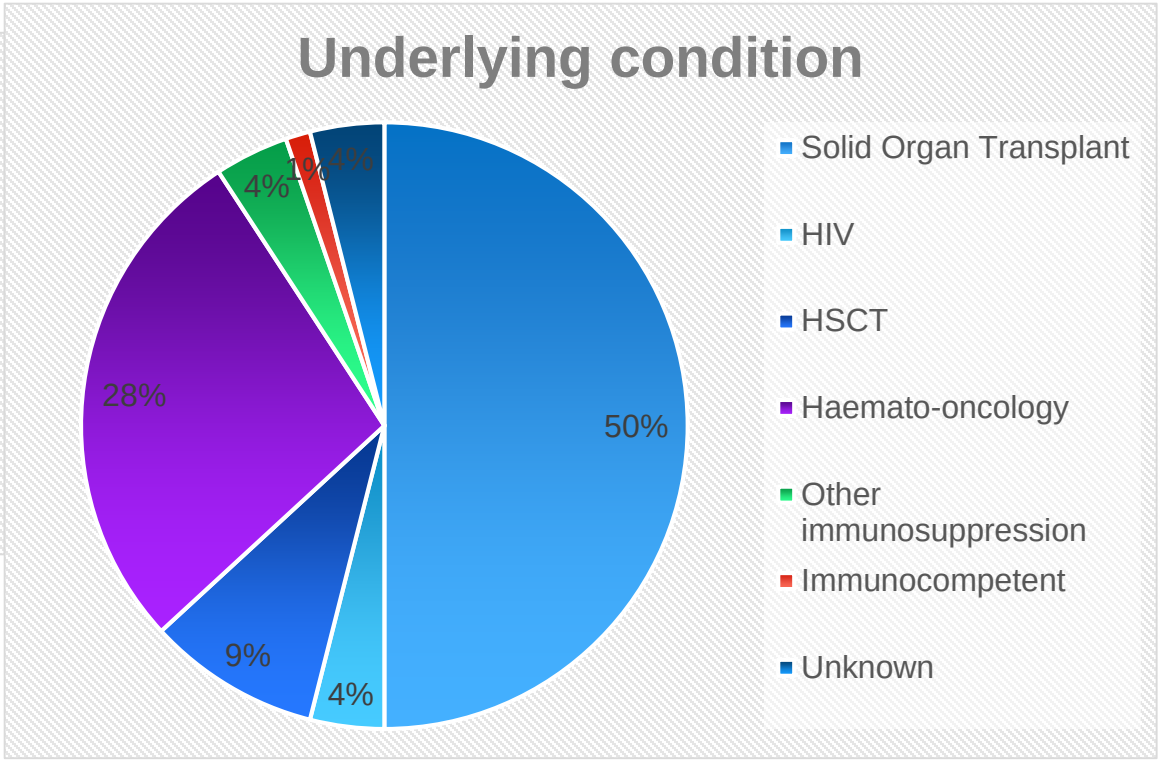
Patients with chronic HEV, 2009 to 2016 (n=76)





Blood donor screening within NHSBT

NHS Blood and Transplant

- NHSBT began screening in February 2016
- Pools of 24 donations, reactive pools resolved to the individual donation
- Confirmation of HEV RNA reactivity using an in-house real time PCR assay and serology
- Whole blood donors deferred for 6 months with automatic re-instatement
- Component donors deferred until RNA negative and IgG positive (>10IU/ml)
  - Follow up at 6 weeks if Ab positive at donation
  - Follow up at 8 weeks if Ab negative at donation
  - Archive of previous donation tested for HEV RNA

HEV – UK Timeline

NHS Blood and Transplant

2006
- First reported case of Transfusion-Transmitted HEV in UK

2010
- Steady increase of indigenous HEV in the UK
- HEV genotype 3, clade 2 on the rise

2012
- Reports of potential TTI cases to NHSBT begin to increase
- NHSBT/PHE HEV Prevalence and Transmission Study begins

2014
- NHSBT/PHE HEV Prevalence and Transmission Study is published
- **SABTO 1st HEV Working Group**

2015
- **SABTO Guidance** – Screened components for stem cells and solid organ transplant recipients
- Increase in HEV case ascertainment in immunocompromised patients

2016
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2017
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- HEV NAT screening of NHSBT stem cell, tissue and organ donors to be implemented in Autumn

NHS
Blood and Transplant

Which patients need to be protected from HEV infection? (2)

- Patients who have received a haematopoietic stem cell transplant for at least 12 months after finishing all immunosuppressive treatment or longer where the patient has developed graft versus host disease
- Patients receiving other types of immunosuppressive drugs, either alone or in combination with lower doses of steroids, until at least 6 months after terminating such treatment

NHS Blood and Transplant

Which patients need to be protected from HEV infection? (3)

- Patients who are immunocompromised due to Human Immunodeficiency Virus (HIV) infection with a CD4 count of <200mm^3
- Patients who are within three months of a planned elective organ transplant and patients who may receive a solid organ transplant within three months due to being on the UK national transplant waiting list.The provision of HEV screened components includes those components used in organ perfusion