

# 17 Transfusion-Transmitted Infections (TTI) n=1

*Authors: Rachael Morrison and Su Brailsford*

## Definition of a TTI:

A report was classified as a transfusion-transmitted infection if, following investigation:

- The recipient had evidence of infection following transfusion with blood components, and there was no evidence of infection prior to transfusion, and no evidence of an alternative source of infection

and either:

- At least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection

or:

- At least one component received by the infected recipient was shown to contain the agent of infection

Note that for the purposes of the European Union (EU) legislation, serious adverse reactions (SAR) are defined as any reactions in patients that are 'life-threatening, disabling or incapacitating, or which result in or prolong hospitalisation or morbidity.'

These must be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) (a legal requirement). This includes all confirmed transfusion-transmitted infections.

## Key SHOT messages

- Bacterial screening of platelets has been shown to be useful in reducing the risk of contaminated platelets entering the blood supply, however, there is still a small residual risk that bacteria may not be detected
- The risk of transfusion-transmitted hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV) is very low in the UK
- Clinicians investigating suspected viral TTI should explore all possible risk exposures in parallel with the Blood Service investigations, in order to determine the patient's most likely source of infection. For example, hepatitis E virus (HEV) is commonly transmitted by food. Investigation includes checking records and if available, testing samples, including non-transfusion samples, taken prior to the implicated transfusion(s) to check that the recipient did not already have infection

## Introduction

This chapter describes the possible transfusion-transmitted infection incidents investigated by the United Kingdom (UK) Blood Services and reported to the National Health Service Blood and Transplant (NHSBT)/Public Health England (PHE) Epidemiology Unit in 2016.

## Summary of reports made to the NHSBT/PHE Epidemiology Unit in 2016

During 2016, UK Blood Services investigated 108 suspected bacterial cases and 18 suspected viral incidents (Figure 17.1). From these suspected cases, there have been:

- One transfusion-transmitted HEV incident, following multiple transfusions between October 2015 and January 2016
- Three bacterial near miss incidents from Northern Ireland
- One bacterial near miss incident in England

Further information about how and what to report can be found in 'SHOT Bites no. 7 Transfusion-transmitted infections' at <https://www.shotuk.org/wp-content/uploads/SHOT-Bites-No7-TTI.pdf>

### Major morbidity n=1

A patient with a confirmed case of transfusion-transmitted HEV suffered a serious reaction (Case 17.5).

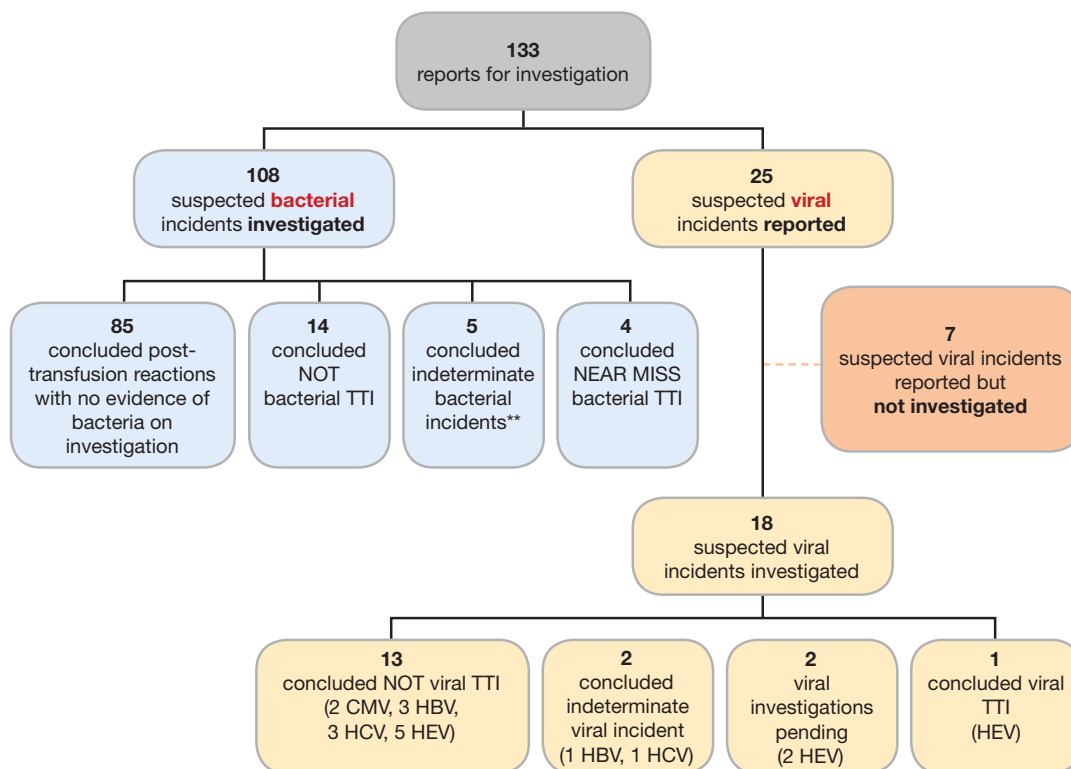


Figure 17.1:  
Outcome of reports  
of suspected  
TTI made to the  
NHSBT/PHE  
Epidemiology Unit  
in 2016\*

\*HCV investigations where the transfusion was prior to screening are not included in the above Figure (2 HCV incidents in 2016)

\*\*No packs to test but investigation based on information received indicates unlikely to reflect a TTI

CMV=cytomegalovirus

### Bacterial TTI reports 2016

In 2016, there were no reported and confirmed bacterial transfusion-transmitted infections, however there were three near miss incidents reported by the Northern Ireland Blood Transfusion Service (NIBTS) of which two occurred in 2016 and one in 2014, and one near miss event in 2016 reported by NHSBT. The four UK Blood Services all use the BacT/ALERT system for bacterial screening but each country uses different methods for sampling platelet packs as shown in Table 17.1. For example NHSBT is the only Blood Service that samples each split apheresis pack; the Welsh Blood Service resamples platelets at day 4 to prolong the shelf life and NIBTS do not sample the packs until 48 hours have passed since donation.

**Case 17.1: Near miss 1**

*One unit of apheresis platelets was issued and transfused as a 3-day-old pack without event. Pack 2 of the same donation was requested for the same patient, however, on inspection prior to transfusion, staff noted a clump of material in the 5-day-old pack and returned the pack to NIBTS for investigation. Staphylococcus aureus was isolated from pack 2, bacterial screening results for both packs were negative at day 7. The donor was a regular donor who had given over 100 platelet donations. The donor was recalled and permission given for samples to be taken including peripheral blood cultures and swabs from the antecubital fossa (venepuncture site, pre and post cleansing) nasal and oral cavities; axilla; and inguinal areas. Staphylococcus aureus was only cultured from the left nostril. Molecular typing gave indistinguishable results for the isolates from both the pack and the donor and as such represent a single strain. The donor was permanently withdrawn.*

**Case 17.2: Near miss 2**

*Packs 1, 2 and 3 of an apheresis platelet donation were issued on day 3 to a local hospital. Pack 3 was transfused without any symptoms or signs of a transfusion reaction. Pack 2 was requested for another patient, however, clumps of white material were noted in the platelet pack by one of the nursing team prior to transfusion. Platelet packs 1 and 2 were returned to NIBTS. The donor was a regular donor with no obvious ill health. All three packs were negative on bacterial screening at day 7. Pack 1 was retested and was negative. Pack 2 was re-sampled and cultured and Staphylococcus aureus confirmed. The donor was recalled for samples and peripheral blood cultures and swabs were taken from the antecubital fossa (venepuncture site – pre and post cleansing) nasal and oral cavities; axilla; and inguinal areas. Staphylococcus aureus was not isolated from the blood cultures or skin swabs of the donor. The donor has been temporarily deferred until the investigation concludes.*

**Case 17.3: Near miss 3**

*Two packs of apheresis platelets from one donation were received at one of the NHSBT stock-holding sites. One of the platelet packs looked abnormal and was described as looking like ‘scrambled egg in orange juice’. Pack 2 appeared normal on visual inspection. Both units were returned for bacteriological investigation. Small Gram-negative rods were seen on Gram stain from the index, visually abnormal pack, and the organism was subsequently identified as Serratia marcescens. All processes were reviewed and no errors observed. The donor was a regular donor who was well at the time of donation. The most likely source of contamination was thought to be environmental whereas a subclinical infection in the donor was less likely. The implicated platelet pack was sent for pressure testing to exclude this as a source of the contamination, there was no evidence of any leaks. Environmental monitoring records of both the donor centre and manufacturing site were checked and found to be as expected. Despite extensive investigations no obvious source of the contamination was found.*

**Case 17.4: Near miss case from 2014**

*Transfusion laboratory staff noted obvious visible clumping in a day 6 apheresis platelet pack (pack 1). Cultures of both aerobic and anaerobic BacT/ALERT samples were negative at 12 days. The pack was resampled and Staphylococcus aureus was confirmed on resampling from pack 1 only. Pack 2 was negative on resampling. The donor was recalled and a number of skin abrasions were noted, the donor had recently played rugby. Swabs and peripheral blood cultures were taken from the donor and Staphylococcus aureus was isolated from the left nasal cavity. Molecular typing showed the pack and donor isolated were indistinguishable. The donor was permanently removed from active panel.*

**Bacterial TTI 1996 – 2016**

Screening of platelet components cannot guarantee freedom from bacterial contamination. Packs are released for issue as ‘negative-to-date’ which may be before bacteria have multiplied sufficiently to trigger an initial screening reaction. On the other hand, an initial screen reactive result may be a false positive result, or related to bacteria which are of low pathogenicity and unlikely to cause any noticeable reaction in the recipient. The last confirmed bacterial TTI was in 2015. Prior to 2015, the previous

documented confirmed bacterial TTI was in 2009, predating universal bacterial screening of platelets throughout the UK Blood Services (2011). There have been 8 near misses (7 in platelets) reported to the unit between 2011 and 2016. Overall, a total of 37/44 bacterial transfusion-transmissions to individual recipients (34 incidents) have been caused by the transfusion of platelets, and 7/44 by red cells (Table 17.3) since reporting began.

Haemovigilance systems for bacterial TTI are passive and as such rely on clinical colleagues to report suspected TTI. Following the introduction of bacterial screening of platelets, colleagues were reminded that there was still the possibility of TTI occurring from both platelet and red cell transfusion and the numbers of reported suspected TTI have remained almost constant. Current British Society for Haematology (BSH) guidance recommends that patients are advised to report any symptoms that occur within 24 hours of transfusion (BSH Tinegate et al. 2012) although our experience suggests that patients with confirmed TTI become unwell very rapidly. Within NHSBT, post-dated platelets are randomly sampled for the presence of bacteria, and to date, there is no evidence that bacterial screening is routinely failing to detect potentially pathogenic bacteria.

	Time of sampling (hour)	Volume sampled (mL)	Apheresis sample	Time at release (hour)	Length of screening
NHSBT	36	2 x 8	Post-split	6	Day 7
NIBTS	48	2 x 8	Pre-split	6	Day 9
SNBTS	18	2 x 7	Pre-split	6	Day 7
WBS	16	2 x 10	Pre-split	From start of screening	Day 7*

\*Additional 10mL sample taken at day 4 to extend shelf-life from 5 to 7 days

**Table 17.1:**  
Bacterial screening methods used by the UK Blood Services

## Viral TTI reports 2016

In 2016, there was one confirmed transfusion-transmitted HEV incident.

### Case 17.5: Confirmed viral HEV TTI case (major morbidity)

*A male patient in his 70's with a diagnosis of aplastic anaemia was receiving regular blood transfusions with two units of red cells every month. In February 2016 the patient was found to have abnormal liver function tests (LFT). A blood sample was reported in March 2016 as anti-HEV IgM and IgG positive and ribonucleic acid (RNA) positive with a viral load of 410,000 IU/mL. Records of all donors of the implicated packs were examined and archive samples of the donations transfused between December 2015 and January 2016 were retrieved and tested (6 donors); all tested HEV RNA negative. Earlier transfusions given between October to November 2015 were then investigated (4 donors); one of the samples from a donor who donated in October 2015 was confirmed to be HEV RNA positive with a viral load of 3574 IU/mL. The donor cleared the infection and remains on the donor panel.*

### Update on viral TTI reports from 2015

There were two pending HCV and one HEV case in 2015, all of which were found to be NOT a viral TTI.

### Viral TTI 1996 to 2016

The year of transfusion may be many years prior to the year in which the case is investigated and reported to SHOT because of the chronic nature, and therefore late recognition, of some viral infections. Since 1996, 30 confirmed incidents of transfusion-transmitted viral infections have been documented, involving a total of 37 recipients. HBV is the most commonly reported proven viral TTI in the UK. This is partly because the 'window period' where an infectious donation from a recently infected donor cannot be detected by the screening tests is longer than for HCV or HIV, despite nucleic acid testing (NAT).

## Risks of HBV, HCV or HIV being transmitted by transfusion

The risks of a potentially infectious HBV, HCV or HIV window period donation not being detected on testing in the UK are very low (Table 17.2) (PHE 2016).

**Table 17.2:**  
The estimated risk of a potentially infectious HBV, HCV or HIV window period\* donation entering the UK blood supply: 2013-2015

	HBV	HCV	HIV
Number per million donations	0.79	0.025	0.18
95% confidence interval	0.22-1.30	0.01-0.04	0.12-0.27
At 2.3 million donations per year testing will miss a potentially infectious window period donation every:	0.6 years	19-20 years	2-3 years

\*The window period is the time at the start of an infection before the tests can detect it

Fewer TTI are observed in practice than estimated in Table 17.2, partly because the estimates have wide uncertainty and the model is based on the risk in all donations tested. The model does not incorporate pack non-use, recipient susceptibility to infection, or under ascertainment/under reporting, for example due to recipients dying from an underlying medical condition before a chronic asymptomatic viral condition is identified, or, in the case of HBV, an asymptomatic acute infection.

## HEV testing 2017

Following a review by the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO 2016) in October 2016, UK Blood Services have implemented 100% HEV-screening. 100% HEV-screened red cells were available in England from 1<sup>st</sup> May, from 3<sup>rd</sup> April in Wales, and in Scotland from 5<sup>th</sup> April 2017. Replacement of frozen components followed as stocks were used up.

## Parasitic TTI

There were no reported parasitic infections for investigation in 2016. There have been two proven malaria TTI reported to SHOT, the last in 2003 (Table 17.3). Malaria antibody testing was not applicable at the time according to information supplied at donation, and the donor selection guidelines were updated after these incidents to minimise the risk of further malaria TTI (Kitchen et al. 2005). The current selection guidelines on deferral and additional testing for malaria can be accessed at the UK transfusion guidelines web pages at <http://www.transfusinguidelines.org.uk/red-book>.

## Variant Creutzfeldt-Jakob Disease (vCJD) 2016

There were no vCJD investigations in 2016.

## vCJD 1996-2016

Three vCJD incidents (Table 17.3) took place prior to the introduction of leucodepletion and other measures taken by the UK Blood Services to reduce the risk of vCJD transmission by blood, plasma and tissue products. All these measures have been reviewed and endorsed by SaBTO (SABTOa 2013). Risk assessment and research into vCJD continues however currently there is no suitable blood test available for screening blood donations for vCJD.

More information can be found here [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/407681/measures-vcjd.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/407681/measures-vcjd.pdf).

Year of transfusion**	Number of incidents (recipients) by infection											Implicated component				
	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV I	Parvovirus (B19)	Malaria	vCJD/prion	Total	RBC	Pooled platelet	Apheresis platelet	FFP	Cryo
Pre 1996	-	-	1 (1)	-	-	-	2 (2)	-	-	-	3 (3)	3	-	-	-	-
1996	-	1 (1)	1 (1)	1 (1)	-	1 (3)	-	-	-	1 (1)	5 (7)	5	1	-	1	-
1997	3 (3)	-	1 (1)	1 (1)	-	-	-	-	1 (1)	2 (2)	8 (8)	6	1	1	-	-
1998	4 (4)	-	1 (1)	-	-	-	-	-	-	-	5 (5)	2	1	2	-	-
1999	4 (4)	-	2 (3)	-	-	-	-	-	-	‡ (1)	6 (8)	5	3	-	-	-
2000	7 (7)	1 (1)	1 (1)	-	-	-	-	-	-	-	9 (9)	1	5	3	-	-
2001	5 (5)	-	-	-	-	-	-	-	-	-	5 (5)	-	4	1	-	-
2002	1 (1)	-	1 (1)	-	-	1 (1)†	-	-	-	-	3 (3)	2	1	-	-	-
2003	3 (3)	-	1 (1)	-	-	-	-	-	1 (1)	-	5 (5)	1	1	3	-	-
2004	††	-	-	-	1 (1)	-	-	-	-	-	1 (1)	1	-	-	-	-
2005	2 (2)	1 (1)	1 (1)	-	-	-	-	-	-	-	4 (4)	1	3	-	-	-
2006	2 (2)	-	-	-	-	-	-	-	-	-	2 (2)	-	1	1	-	-
2007	3 (3)	-	-	-	-	-	-	-	-	-	3 (3)	2	1	-	-	-
2008	4 (6)	-	-	-	-	-	-	-	-	-	4 (6)	-	2	4	-	-
2009	2 (3)	-	-	-	-	-	-	-	-	-	2 (3)	1	-	2	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	1 (2)	-	1 (2)	-	-	-	-	-	2 (4)	2	-	-	2	-
2012	-	-	1 (1)	-	1 (1)	-	-	1 (1)	-	-	3 (3)	2	-	-	1	-
2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2014	-	-	-	-	2 (3)	-	-	-	-	-	2 (3)	1	-	-	2	-
2015	1 (1)	-	-	-	2 (3)	-	-	-	-	-	3 (4)	-	2	1	-	1
2016	-	-	-	-	1 (1)	-	-	-	-	-	1 (1)	1	-	-	-	-
<b>Number of incidents</b>	<b>41</b>	<b>3</b>	<b>12</b>	<b>2</b>	<b>8</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>76</b>					
Number of infected recipients	44	3	14	2	11	4	2	1	2	4	87	36	26	18	6	1
Death due to, or contributed to, by TTI	11	-	-	-	1	-	-	-	1	3	16					
Major morbidity	29	2	14	2	6	4	2	1	1	1§	62					
Minor morbidity	4	1	-	-	4	-	-	-	-	-	9					
<b>Implicated component</b>																
RBC	7	1	11	2	4	2	2	1	2	4	36					
Pooled platelet	21	2	1	-	1	1	-	-	-	-	26					
Apheresis platelet	16	-	1	-	1	-	-	-	-	-	18					
FFP	-	-	1	-	4	1	-	-	-	-	6					
Cryoprecipitate	-	-	-	-	1	-	-	-	-	-	1					

Numbers in brackets refer to recipients

\*No screening was in place for vCJD, human T cell lymphotropic virus (HTLV), hepatitis A virus (HAV), HEV or parvovirus B19 at the time of the documented transmissions. In both malaria transmissions, malaria antibody testing was not applicable at the time according to information supplied at donation

\*\*Year of transfusion may be prior to year of report to SHOT due to delay in recognition of chronic infection

\*\*\*HCV investigations where the transfusion was prior to screening are not included in the above Figure

†The two HIV incidents were associated with window period donations (anti-HIV negative/HIV RNA positive) before HIV NAT screening was in place. A third window period donation in 2002 was transfused to an elderly patient, who died soon after surgery. The recipient's HIV status was therefore not determined and not included

††In 2004 there was an incident involving contamination of a pooled platelet pack with *Staphylococcus epidermidis*, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely. This case was classified as 'not transfusion-transmitted'

‡Same blood donor as one of the 1997 transmissions so counted as the same incident; note: counted as two separate incidents in previous reports

§A further prion case died but transfusion was not implicated as the cause of death. The outcome was assigned to major morbidity instead because although there was post-mortem evidence of abnormal prion proteins in the spleen the patient had died of a condition unrelated to vCJD and had shown no symptoms of vCJD prior to death

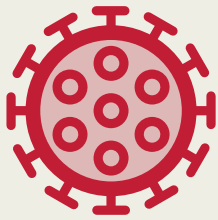
Table 17.3:  
Number of confirmed TTI incidents\*, by year of transfusion\*\* with total infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2016 (Scotland included from October 1998)

## Safe supplies: A picture for policy

Joint working of NHS Blood and Transplant and Public Health England

# Blood donations UK, 2015

**The risk that testing would NOT detect a HBV, HCV or HIV infection is less than one in a million**



	Estimated that testing would NOT detect an infection every:	Last proven transfusion-transmitted infections in the UK
Hepatitis B	8 months	2012
Hepatitis C	19 years	1999
HIV	2-3 years	2002

**42 million**



Age 17-66  
years in  
the UK

**2.1 million**

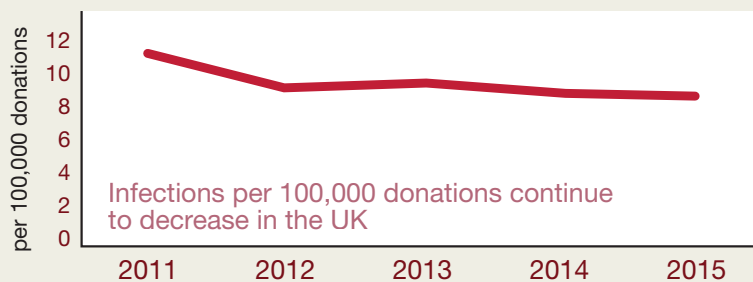


Blood and  
platelet  
donations

**199 infections  
detected**



Mostly chronic  
hepatitis B and  
syphilis

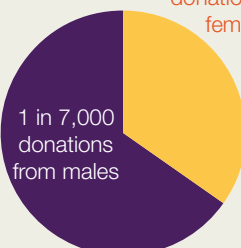


**64** Hepatitis B  
**64** Syphilis  
**49** Hepatitis C  
**13** HIV  
**9** HTLV

1 in 55,000  
donations from  
repeat donors

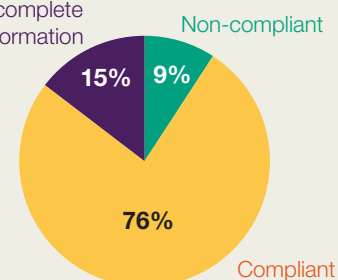


1 in 17,000  
donations from  
females



**Infections more common in new donors and male donors**

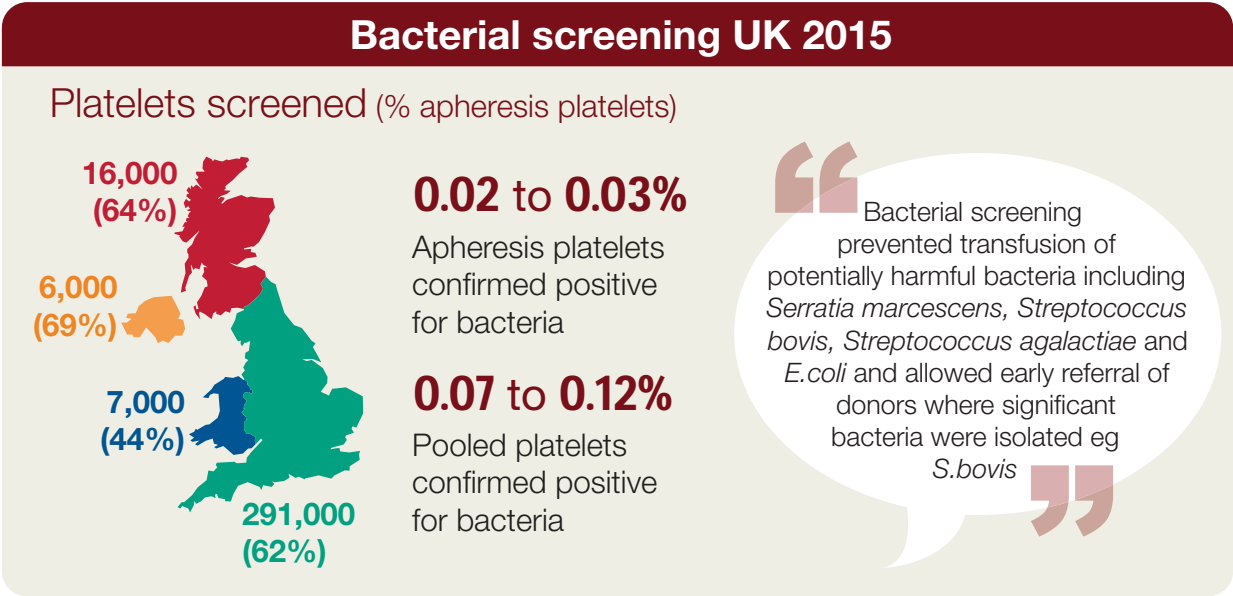
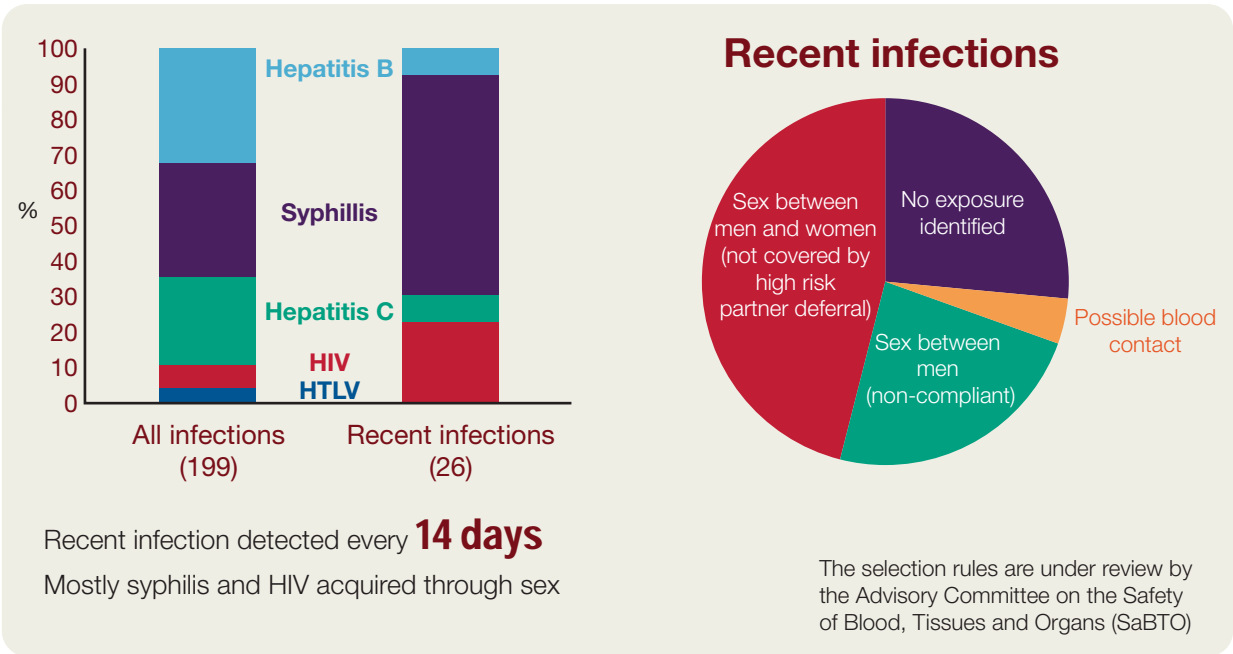
Not known,  
incomplete  
information



Most positive donors had complied  
with the donor selection rules

PHE publications gateway number: 2016xxx





Additional testing NHSBT			
	Instead of travel deferrals		
		Tested 67,000	POSITIVE
			0/1460 Chagas disease    490/27,090 Malaria    0/38,392 West Nile virus
		4%	Donations gained through additional testing

Data source: Data supplied to the NHSBT/PHE Epidemiology Unit by NHSBT, WBS, NIBTS & SNBTS.

PHE publications gateway number: 2016453  
© Crown copyright



For further information or alternative breakdown of data please contact the National Coordinator for Transfusion-Transmitted Infections via the NHSBT/PHE Epidemiology Unit at [epidemiology@nhsbt.nhs.uk](mailto:epidemiology@nhsbt.nhs.uk).

## References

BSH Tinegate H, Birchall J et al. (2012) **Guideline on the investigation and management of acute transfusion reactions**. Br J Haematol 159(2),143-153

Department of Health (2013) **vCJD and transfusion of blood components: an updated risk assessment**. <https://www.gov.uk/government/publications/vcjd-and-transfusion-of-blood-components-updated-risk-assessment> [accessed 24 February 2017]

Hewitt PE, Ijaz S et al. (2014) **Hepatitis E virus in blood components: a prevalence and transmission study in southeast England**. Lancet 384,1766-1773

Kitchen AD, Barbara JA et al. (2005) **Documented cases of post-transfusion malaria occurring in England: a review in relation to current and proposed donor-selection guidelines**. Vox Sang 89,77-80

Parker S, Gil E, et al. (2014) **Case report: passive transfer of hepatitis B antibodies from intravenous immunoglobulin**. BMC Infect Dis 14,99 <http://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-14-99> [accessed 24 February 2017]

PHE (2015) NHSBT/ PHE Epidemiology Unit: **Safe Supplies: A picture for policy**. Annual Review from the NHS Blood and Transplant/Public Health England Epidemiology Unit, 2015. <https://www.gov.uk/government/publications/safe-supplies-annual-review> [accessed 24 February 2017]

SABTO (2012) **Cytomegalovirus tested blood components position statement**. [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/215125/dh\\_133086.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215125/dh_133086.pdf) [accessed 24/02/2017]

SABTOa (2013) **Measures currently in place in the UK to reduce the potential risk of transmitting variant Creutzfeldt-Jakob disease via blood**. <https://www.gov.uk/government/publications/current-measures-to-reduce-the-risk-of-vcjd-transmission-by-blood> [accessed 24 February 2017]

SABTO (2016) **Measures to protect patients from acquiring Hepatitis E virus via transfusion or transplantation**. <http://hospital.blood.co.uk/media/28794/sabto-recommendations-nov-2016.pdf> [accessed 20 March 2017]