JPAC Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee

NHS Blood and Transplant | Northern Ireland Blood Transfusion Service | Scottish National Blood Transfusion Service | Gwasanaeth Gwaed Cymru Welsh Blood Service

What happened to vCJD? The return of UK plasma

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IPFA/PEI May 2024

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Declarations of interest

- No conflicts to declare

- Employed by NHS Blood and Transplant
- Director of JPAC, reporting to UK Forum
- Former member of Advisory Committee on Safety of Blood, Tissues and Organs (SaBTO)

BSE and vCJD

- Bovine Spongiform Encephalopathy probably existed since the 1970s
- First investigated in 1985
- Food chain measures from 1988
- vCJD identified 1996





Mirror

The case was identified as a result of routine surveillance and control measures (Image: AFP)

NEWS | POLITICS | FOOTBALL | CELEBS | TV | SHOPPING | ROYALS

Mad cow disease confirmed on UK farm as urgent restrictions put in place

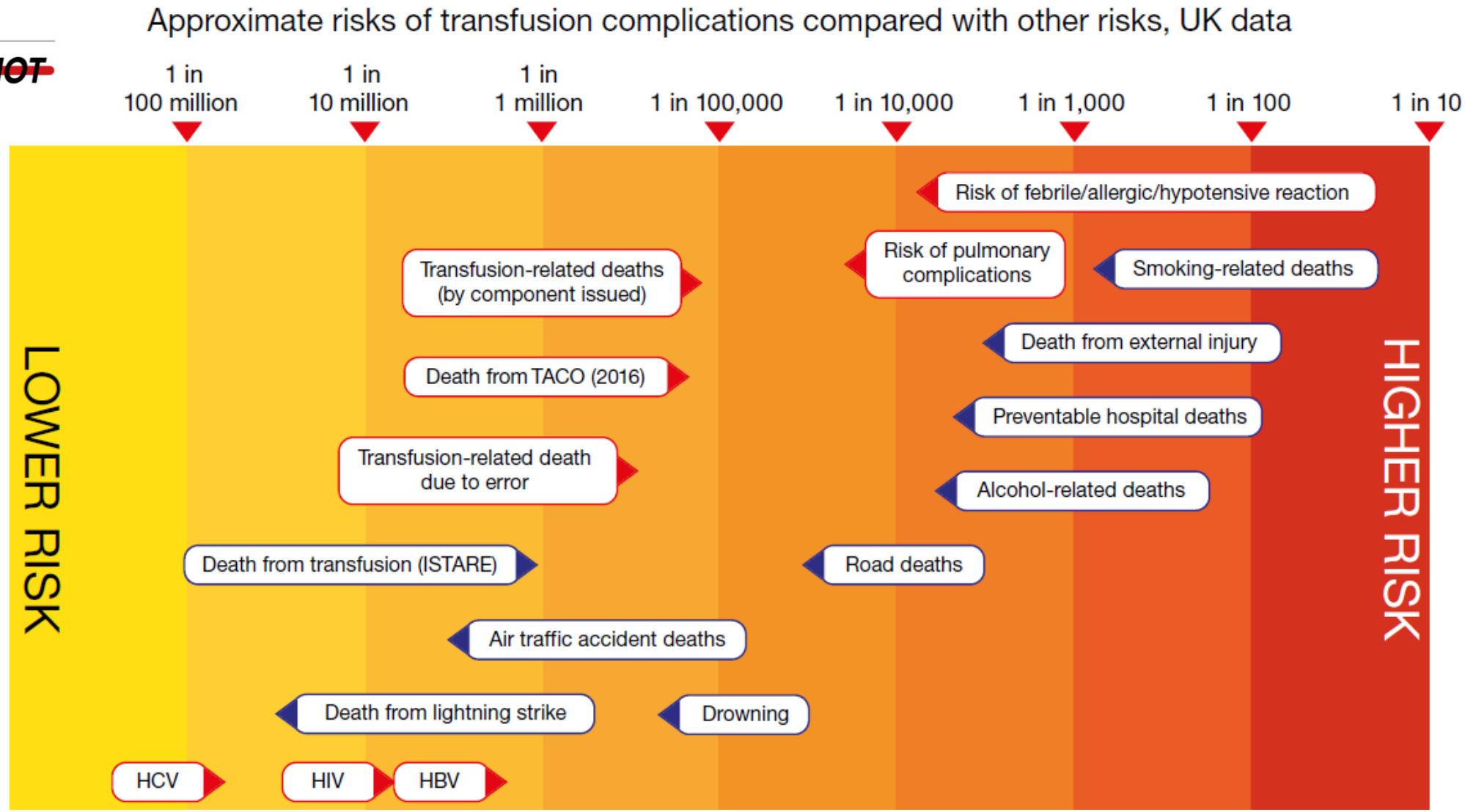
The case of the disease, officially called Bovine Spongiform Encephalopathy (BSE), was discovered on a farm in Ayrshire - the Scottish Government said movement restrictions have been put in place

By Joe Smith, News Reporter
10:48, 10 May 2024 | UPDATED 13:59, 10 MAY 2024

28 | BOOKMARK

https://www.mirror.co.uk/news/uk-news/breaking-case-mad-cow-disease-32778481

Figure 3.8: Risks associated with transfusion compared with other potential life events



Sources of data: Many of these are found online in the UK office for national statistics. Red outline indicates SHOT data, blue outline indicates data from other sources. ISTARE is the International Haemovigilance Network database for the surveillance of adverse reactions and events in donor and recipients. Viral transmissions denote risk of infection, not deaths. HCV=hepatitis C virus; HIV=human immunodeficiency virus; HBV=hepatitis B virus. A full list of sources is available in supplementary information on the SHOT website www.shotuk.org.

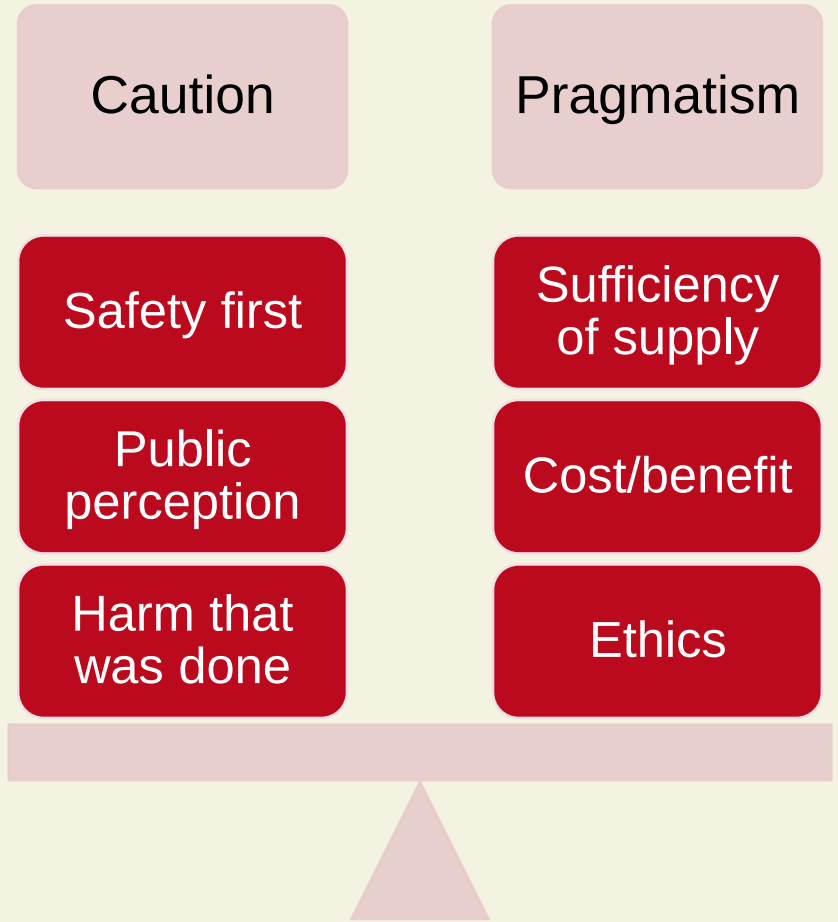
Blood is a special case

- Other healthcare risks are more tolerated
- Precautionary principle

ALLIANCE OF BLOOD OPERATORS

Risk-Based Decision-Making Framework for Blood Safety

https://riskframework.allianceofbloodoperators.org/

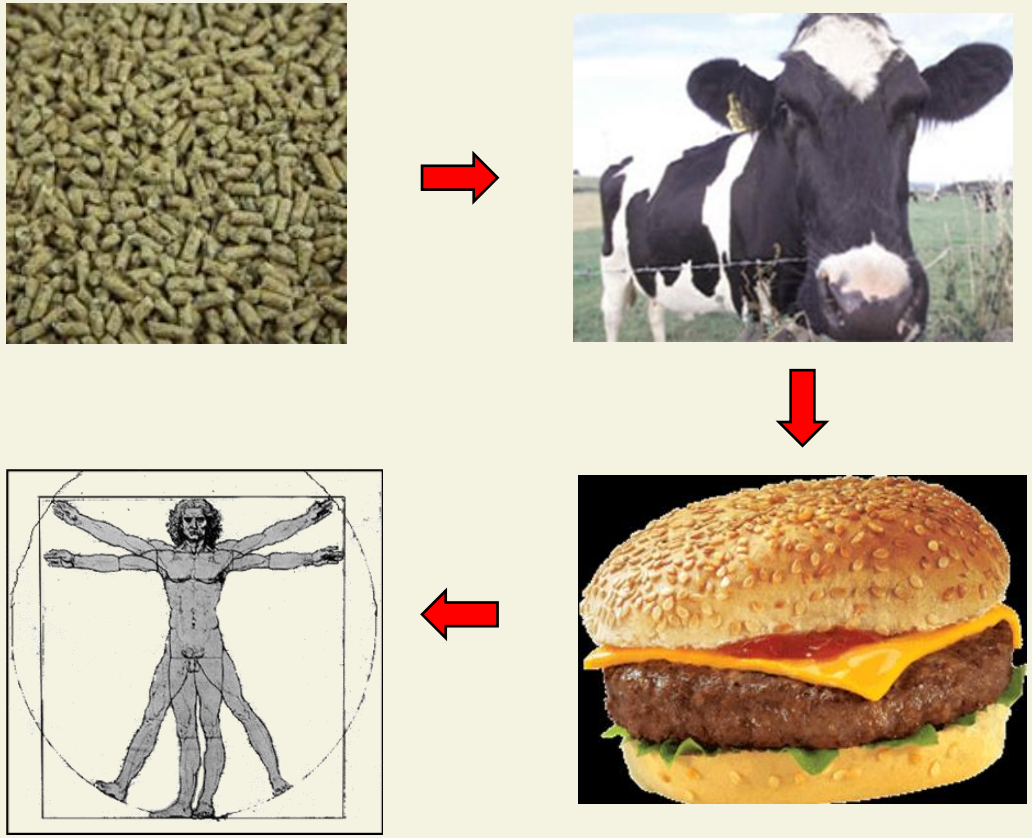


The special case of vCJD

- Prior to 1989 there were ~475k cases of BSE but no crossing of the species barrier to humans

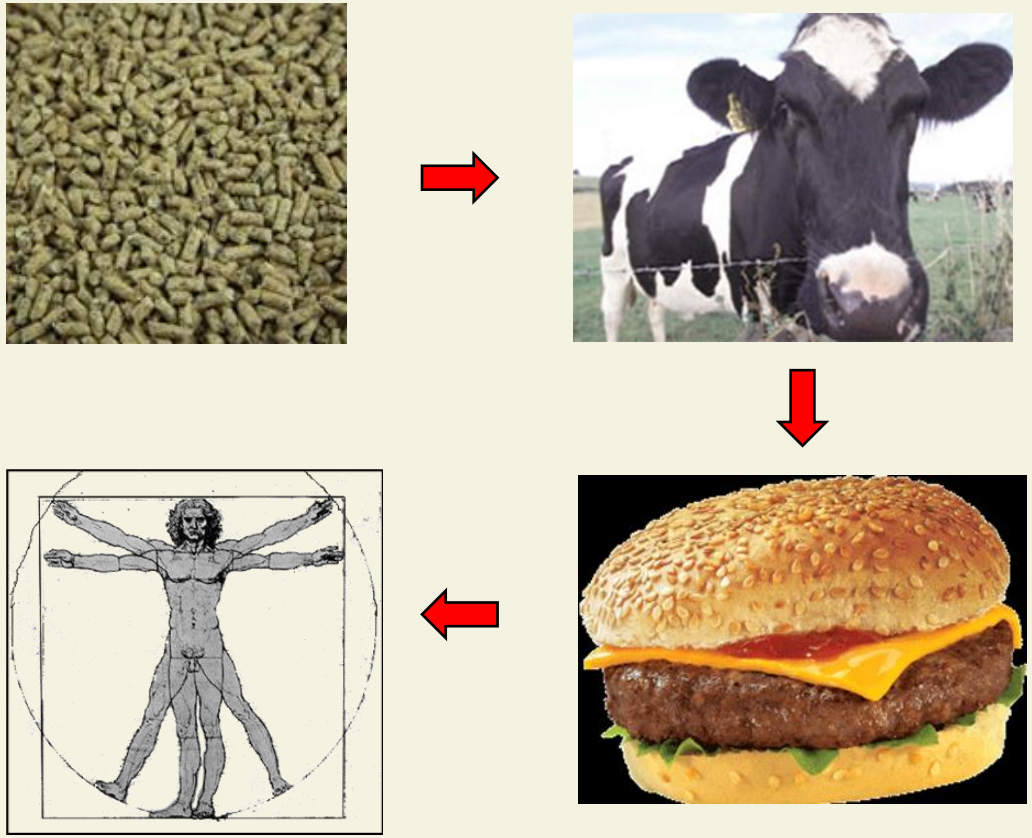
The special case of vCJD

- Prior to 1989 there were ~475k cases of BSE but no crossing of the species barrier to humans



The special case of vCJD

- Prior to 1989 there were ~475k cases of BSE but no crossing of the species barrier to humans
- "BSE is the first man-made epidemic … A human decision to feed meat and bone meal to previously herbivorous cattle … caused what was previously an animal pathogen to enter into the human food chain… causing humans to contract vCJD."



https://en.wikipedia.org/wiki/Variant_Creutzfeldt%E2%80%93Jakob_disease

Impact on blood safety / risk management



"The Government did not lie to the public … it believed that the risks posed by BSE to humans were remote.
The Government was preoccupied with preventing an alarmist over-reaction to BSE.

https://webarchive.nationalarchives.gov.uk/ukgwa/20060525120000/http://www.bseinquiry.gov.uk/index.htm

Impact on blood safety / risk management



Not secure | news.bbc.co.uk/onthisday/hi/dates/stories/may/16/newsid_2913000/2913807.stm

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ON THIS DAY 1950 2005 — 16 May — BBC NEWS

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1990: Gummer enlists daughter in BSE fight

The government has again attempted to reassure the public that British beef is safe, despite growing fears over the cattle disease, Bovine Spongiform Encephalopathy (BSE).

The Minister of Agriculture, John Gummer, even invited newspapers and camera crews to photograph him trying to feed a beefburger to his four-year-old daughter, Cordelia, at an event in his Suffolk constituency.

Although his daughter refused the burger, he took a large bite himself, saying it was "absolutely delicious".

Watch/Listen

John Gummer tried to feed his daughter a beefburger to try to convince the public

PLAY VIDEO

BBC news report on the crisis

Stories From 16 May

- 1943: Germans crush Jewish uprising
- 1974: Dozens die as Israel retaliates for Ma'alot
- 1985: Miners jailed for pit strike murder
- 1968: Three die as tower block collapses
- 1990: Gummer enlists daughter in BSE fight
- 2001: Prescott punches protester

BBC News >>

In depth
The BSE and CJD crisis in the UK

Impact on blood safety / risk management



"The Government did not lie to the public … it believed that the risks posed by BSE to humans were remote.
The Government was preoccupied with preventing an alarmist over-reaction to BSE.

When on 20 March 1996 the Government announced that BSE had probably been transmitted to humans,
the public felt that they had been betrayed.

Confidence in government pronouncements about risk was a further casualty of BSE."

https://webarchive.nationalarchives.gov.uk/ukgwa/20060525120000/http://www.bseinquiry.gov.uk/index.htm

Protecting the food chain (since 1996)

- Strict controls in place to stop BSE entering the human food chain, including:
  - a ban on feeding meat-and-bone mix to farm animals
  - the removal and destruction of all parts of an animal's carcass that could be infected with BSE
  - a ban on mechanically recovered meat
  - testing on all cattle more than 30 months old

https://www.nhs.uk/conditions/creutzfeldt-jakob-disease-cjd/prevention/



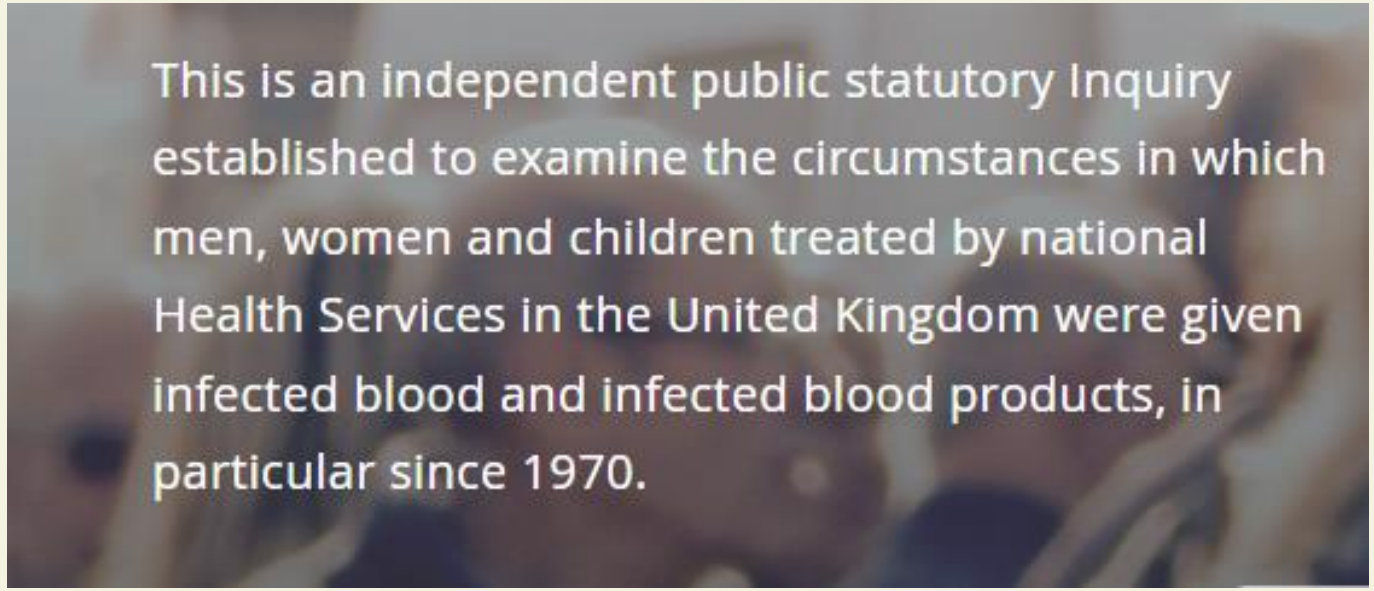


www.theguardian.com

Infected Blood Inquiry (2017 – present)

Report to be published 20 May 2024





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Contaminated blood scandal

May 2024



Infected blood scandal: women with hepatitis C 'dismissed' by doctors

Medical problems blamed on weight, motherhood, menopause or teenage mood swings, say women

14 May 2024



'Why must I be a doctor, solicitor and detective?': lost records block compensation for infected blood victims

12 May 2024

Revealed: key files shredded as UK government panic grew over infected blood deaths lawsuit

5 May 2024

Infected blood inquiry: study that said risk was seen as 'tolerable' omitted patient death

2 May 2024

Ministers agree three-month deadline for UK infected blood compensation

1 May 2024

Protecting patients

TABLE 1 vCJD risk reduction measures implemented in the UK blood supply chain

Year	Risk reduction measure
1997	All blood components, blood products or tissues obtained from any individual who later develops clinical vCJD have been withdrawn/recalled to prevent their use.
1998	Synthetic (recombinant) clotting factor for the treatment of haemophilia provided to those aged under 16 years; since 2005 this measure has been extended to all patients for whom it is clinically appropriate.
1999	White blood cells (thought to contain most of the infectious agent that causes vCJD) have been reduced in all blood components used for transfusion, by a process known as leucodepletion or leucoreduction.
1999	Plasma for the manufacture of medicines such as clotting factors and immunoglobulins has been obtained from non-UK sources.
2004	All individuals who had themselves received a transfusion of blood components (anywhere in the world) since January 1980 were excluded from donating blood.
2004	Plasma for transfusion to those born on or after 1st January 1996 has been obtained from outside the UK.
2005	Provision of platelets collected from a single donor by apheresis provided for transfusion to those born on or after 1st January 1996.
2009	A minimum of 80% of platelets to be collected from single donors by apheresis, for transfusion to all recipients. This measure was reassessed and rescinded in 2013.

Received: 9 July 2021 | Revised: 5 November 2021 | Accepted: 11 November 2021
DOI: 10.1111/tme.12840

REVIEW ARTICLE

TRANSFUSION MEDICINE WILEY

Importation of plasma and use of apheresis platelets as risk reduction measures for variant Creutzfeldt-Jakob disease: The SaBTO review

Stephen Thomas[1] | Matthew Katz[2] | Anne-Marie Slowther[3] | Emily Coelho[2] | Gary Mallinson[4] | Paediatric Components Working Group of the Advisory Committee on the Safety of Blood, Tissues and Organs

Ensuring sufficiency

future cases of vCJD; and cost-effectiveness. The working group recommended that the current vCJD risk reduction measures for individuals born after 1995 or with thrombotic thrombocytopenic purpura (TTP) could be withdrawn. After consultation with stakeholders, SaBTO accepted these proposals which allow more equal provision of components, less operational complexity and risk, and more resources to be deployed elsewhere in the NHS. The potential saving on plasma will be £500 m and moving to using pooled platelets in additive solution for all recipients will bring potential savings of £280 m over the next 50 to 60 years. There could be small number of additional clinical cases of vCJD: 1–2 (<1–14; 95% CI) from plasma and 3–4 (<1 to 45; 95% CI) from platelets. Local and national guidelines will still be applied for managing individual conditions. UK Ministers for Health accepted SaBTO's recommendations on 9 Sept 2019 and implementation began immediately. This paper describes the review and rationale leading to these recommendations.

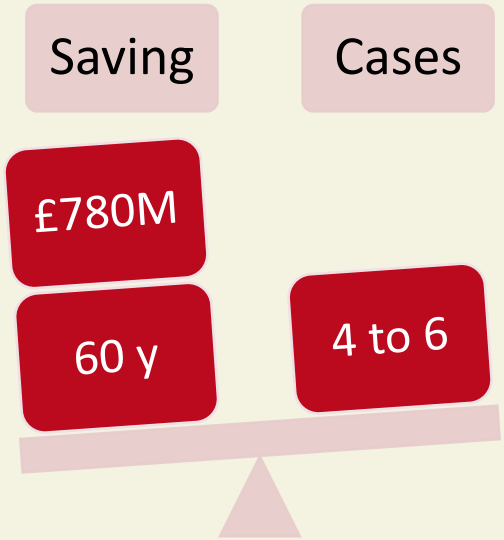
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Demand for PDMPs is increasing

CURRENT OPINION

Global immunoglobulin supply: steaming towards the iceberg?

Johan Prevot[a] *and Stephen Jolles*[b]

Curr Opin Allergy Clin Immunol 2020, 20:557–564
DOI:10.1097/ACI.0000000000000696

KEY POINTS

- The demand for Ig therapies is growing annually at 6–8% across a broad range of indications with particular growth in secondary immunodeficiency.
- There is a significant imbalance in global plasma collection with 65% of this being from the United States with a need for more regionally balanced collection.





Demand for PDMPs is increasing

Received: 22 December 2023 | Revised: 8 March 2024 | Accepted: 10 March 2024

DOI: 10.1111/trf.17801

BRIEF REPORT

TRANSFUSION

A global analysis of the use of immunoglobulin, shortages in supply, and mitigating measures: A survey of hospital providers (a BEST Collaborative study)

Cynthia So-Osman[1] | Meghan Delaney[2] | Mark Fung[3] | Wen Lu[4] | Michael Murphy[5] | Praiseldy Langi Sasongko[6] | Pierre Tiberghien[7,8] | Alan Tinmouth[9] | on behalf of the Best ImmunoGlobulin (BIG) Study Group* the Biomedical Excellence for Safer Transfusion Collaborative

Modelling and decision-making in the UK

Risk modelling

Department of Health and Social Care (DHSC) Analytical Team

Risk assessment

Transmissible Spongiform Encephalitis Risk Assessment Sub-Group (TSE SG)

Risk assessment

Advisory Committee on Dangerous Pathogens (ACDP)

Risk management

Advisory Committee on Safety of Blood, Tissues and Organs (SaBTO)

Output

Paediatric components review

Pending review of current risk reduction measures

Risk management

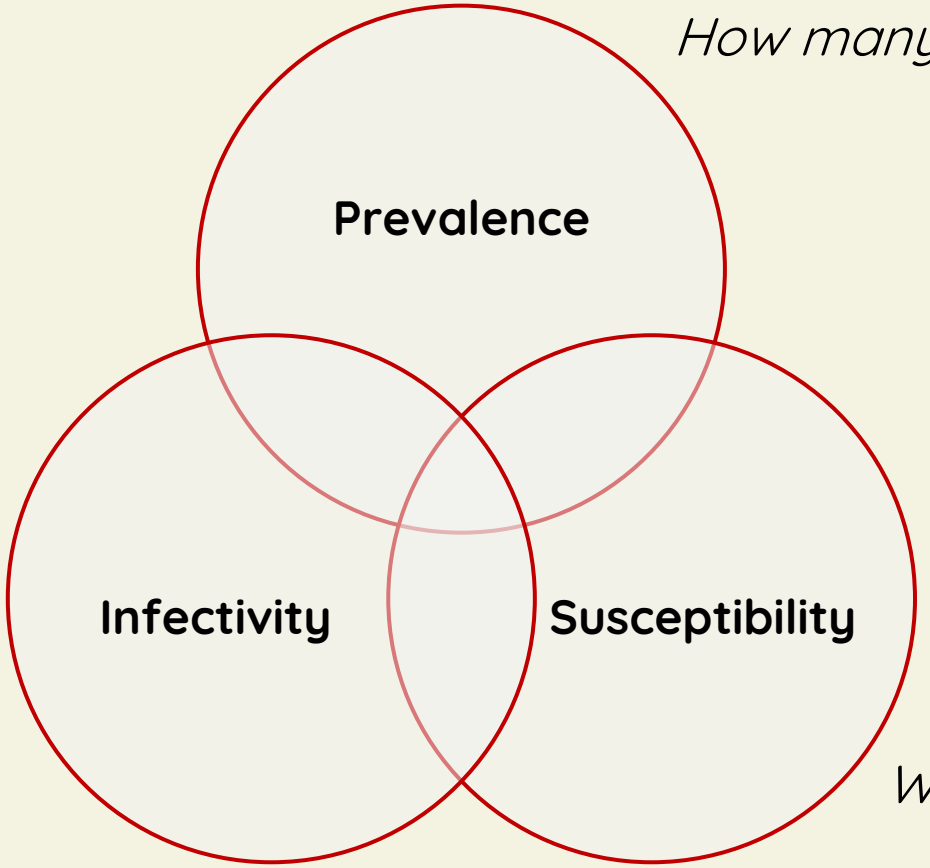
Commission on Human Medicines (CHM)

Output

Licensing of medicines, including the use of UK plasma as a source material for PDMPs

Modelling the risk

How many people have it?



How infectious are they?

Who could catch it?

Prevalence - Appendix I & Appendix II studies

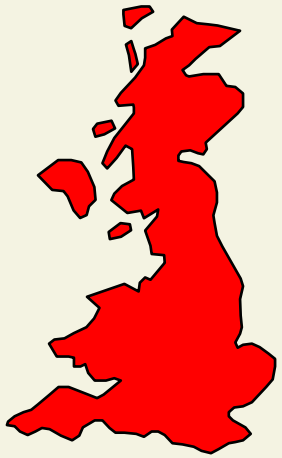
Study	Report	Positives	Total	Rate/10^6 [95% CI]	'Central' rate
Appendix I	Hilton et al J Path 2004	3	12,674	237 [49-692]	1:4000
Appendix II	Gill et al BMJ 2013	16	32,441	493 [282-801]	1:2000

But… is abnormal prion protein in the appendix due to BSE ?



PRE-BSE

Appendices removed < 1979



BSE

1980-1996

Appendix I & II studies

1 in 2000



POST-BSE

Appendices from those born ≥ 1996

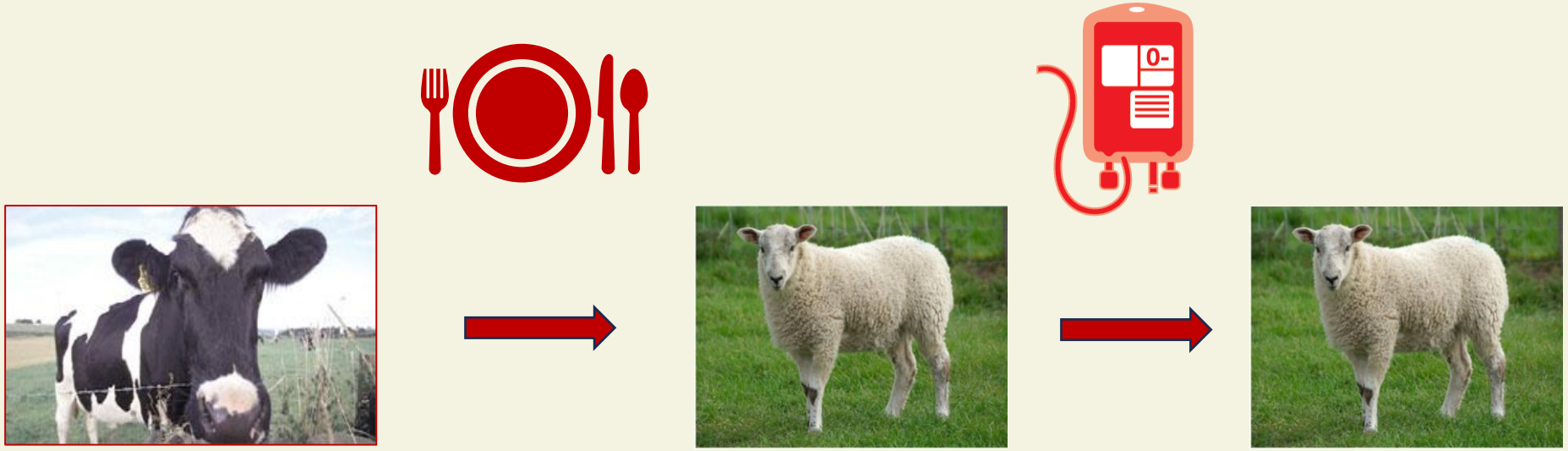
Appendix III study

Appendix III Results (Prevalence)

- No statistically significant difference between the three periods

- Therefore, either:
  - The BSE exposure period was longer than previously thought
    or
  - Abnormal prion protein in the appendix is not BSE-related

Infectivity - BSE sheep transfusion experiments



Infectivity - BSE sheep transfusion experiments

Component	NLD	LD
Whole Blood	50 %	-
Buffy Coat	42 %	-
Platelets	32 %	5 %
Red Cell Concentrate	27 %	14 %
Plasma	19 %	9 %

- All components transmit
- WBCs highest infectivity
- Leucodepletion reduces but does not abolish risk

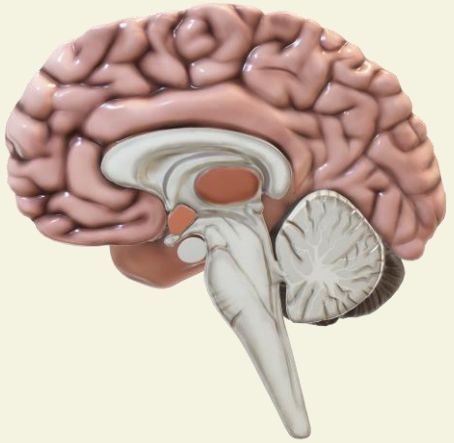
Salamat et al PLoS Pathogens 2021

Observational studies (Susceptibility)

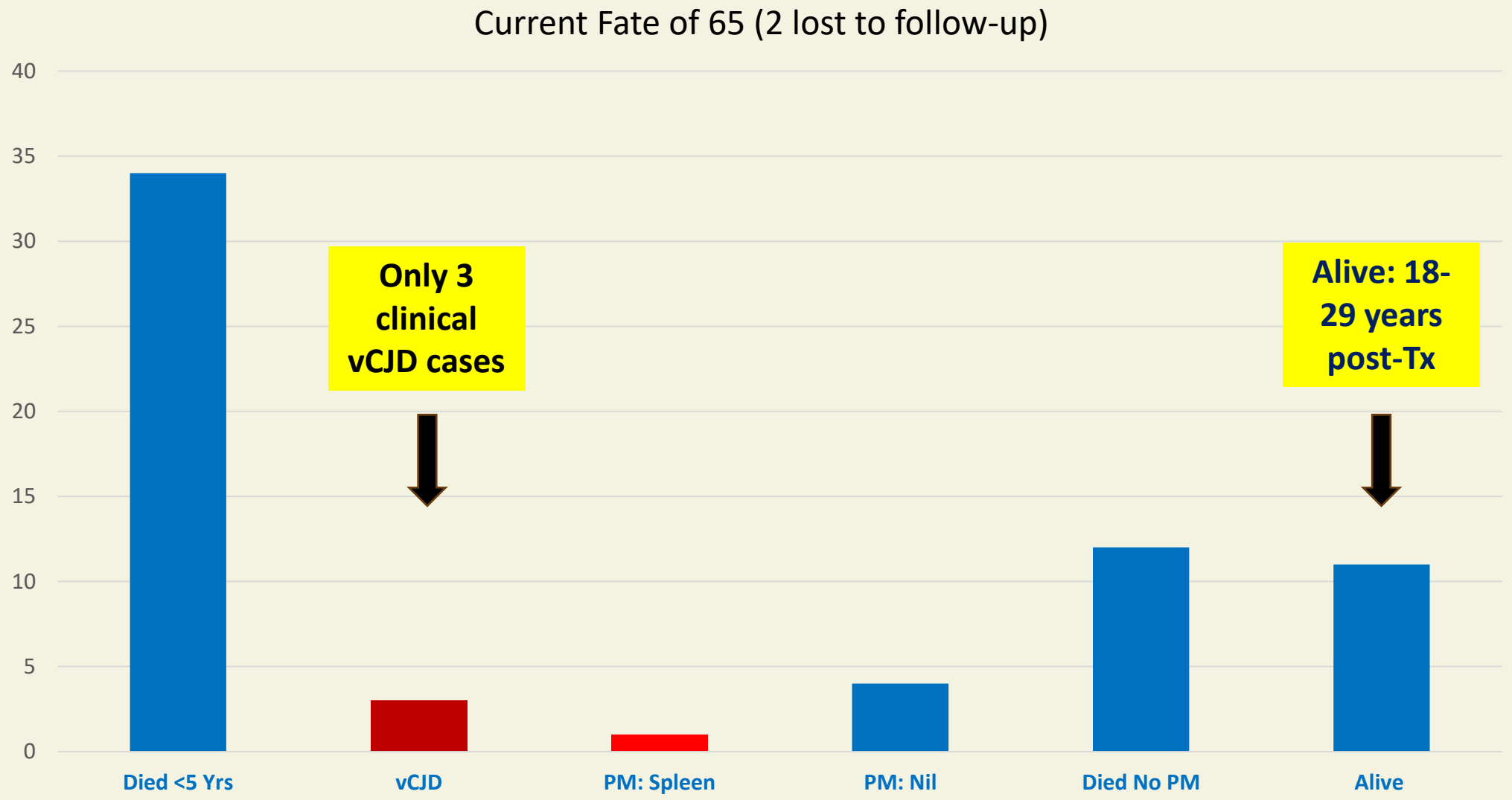
- UK CJD surveillance system
- The ‘Highly Transfused’ study
- The Haemophilia Centres study
- Primary Immunodeficiency Study (PID)
- Transfusion Medicine Epidemiology Review (TMER)







18 vCJD Donors: Traced to 67 Recipients (TMER 2023)



Observational studies (Susceptibility)



- No known living cases of vCJD in the world



- No UK case of vCJD in anyone born after 1989
- Last UK vCJD onset 2014 (death in 2016; n = 178)
- >58 million UK blood components issued since 1999



- No blood/PDMP cases in France (n = 29)



- TTI cases were exposed 1994-1999 (Non-LD RCC)
- No TTI since 1999, none identified since 2007



- Only one case *considered* as PDMP-related (1996)

What does this look like today?

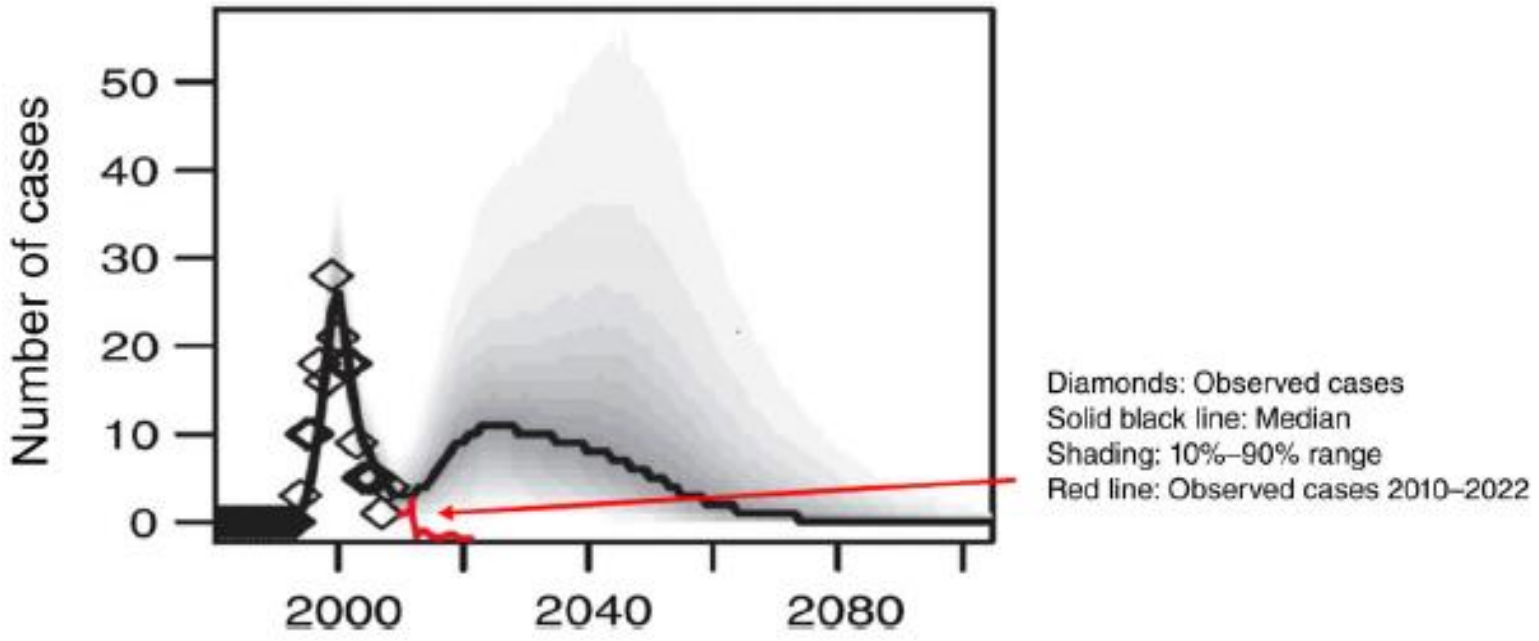


FIGURE 1 Modelling from 2010 predicting a significant second peak of infections. The actual number of cases has been much smaller (adapted from [26]). *Garske T, Ghani AC; PLoS One; 2010 Dec 23; 5(12)*

- 2010 modelling predicted a median of 390 cases (95 % CI 84 – 3000)
- Reality: 178 cases in the UK, 233 worldwide; 1995 – 2016 with a peak in 2000

Why change? Ethics:

- The precautionary principle
  - cannot justify action that will, in any credible scenario, cause more serious harms than it would prevent
- Removal of a safety measure
  - would such a policy be implemented today, based on the latest evidence?



UK Regulatory changes

MHRA 2019

- "The Commission on Human Medicines (CHM) has concluded that the risk of vCJD cases arising from the use of UK plasma for the manufacture of immunoglobulin medicinal products would be **negligible**."



UK Regulatory changes

MHRA 2019 and 2023

- "The Commission on Human Medicines (CHM) has concluded that the risk of vCJD cases arising from the use of UK plasma for the manufacture of immunoglobulin medicinal products would be **negligible**."

- "based on the currently available evidence, it is considered that the use of plasma from UK donors for the manufacture of human albumin products would expose the target patient population to no or **minimal** additional risk of vCJD in the future."



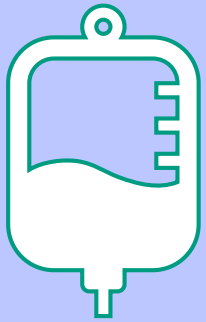


UK Plasma Key Facts



17,000

Number of Ig patients in England



312,000L

Volume of Plasma NHBST is targeting to collect annually



25%

Estimated Ig self-sufficiency at target plasma volumes

Phase 1a: Launch (Jul 2024-Dec 2025)

Target Ig Self-Sufficiency: 25%

Focus: Reinstating a stable and viable supply chain for UK plasma derived medicines.

2023	2024	2025

Manufacturing License — EMA/BWP

Product Licenses — MHRA MAA Review

Mobilisation — NHSBT / Fractionator / NHSE

Supply Plasma — Plasma to Fractionator

Product Availability — Products to Patients





By the end of 2025 we will have;

- Built & stabilised the end-to-end medicinal supply chain, delivering licensed Ig and Albumin products to UK patients.
- Maximised the recovery of plasma from whole blood donations (c280,000-300,000L per annum)
- Demonstrated the ability to achieve source plasma collection at scale and submitted the business case/s for further investment.

Abbreviations Key

European Medicines Agency (**EMA**) Biologics Working Party (**BWP**)

Medicines and Healthcare Products Regulatory Agency (**MHRA**) Marketing Authorisation Application (**MAA**)

Received: 21 December 2022 | Revised: 16 January 2023 | Accepted: 7 February 2023

DOI: 10.1111/vox.13416

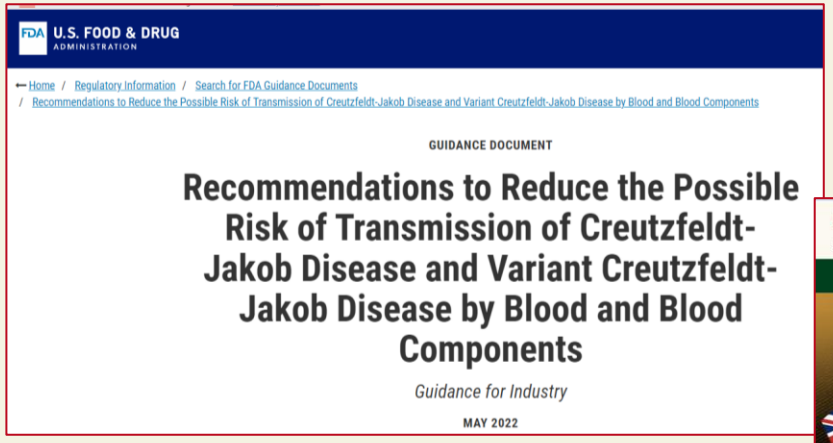
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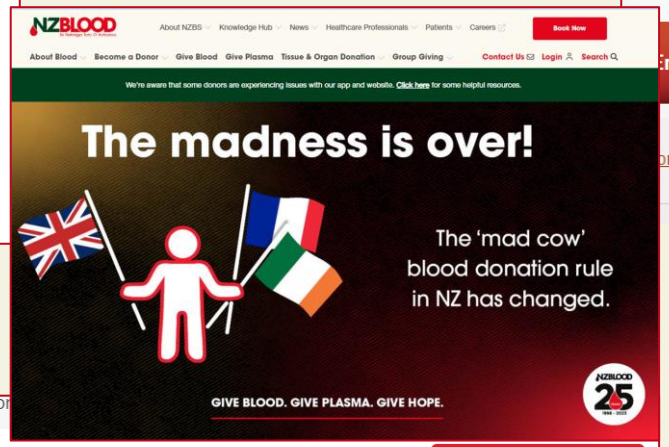
Vox Sanguinis ISBT International Society of Blood Transfusion

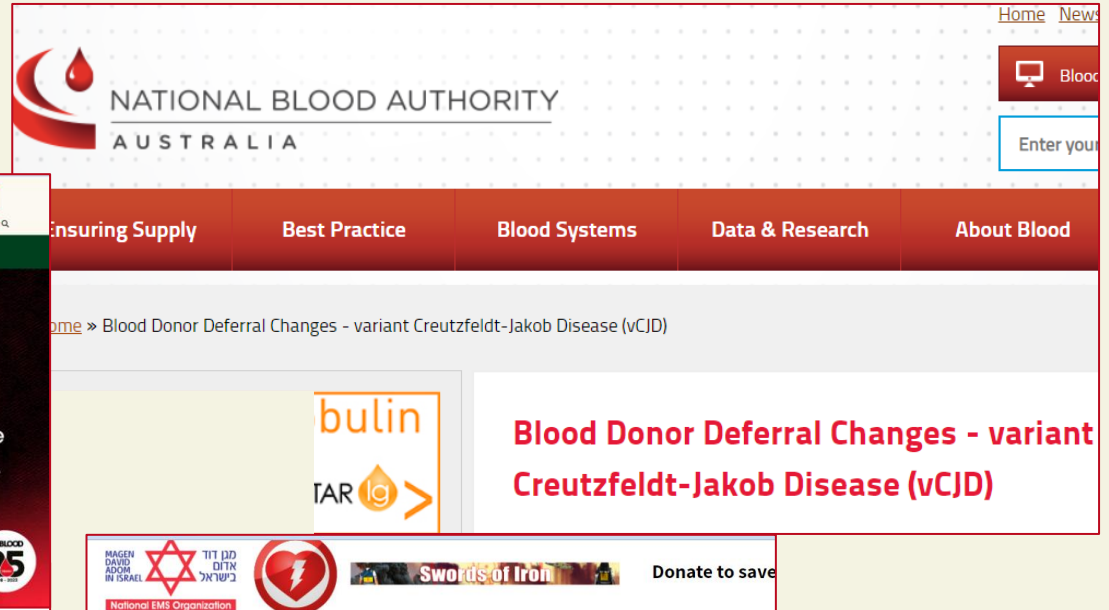
Safety profile of plasma for fractionation donated in the United Kingdom, with respect to variant Creutzfeldt–Jakob disease

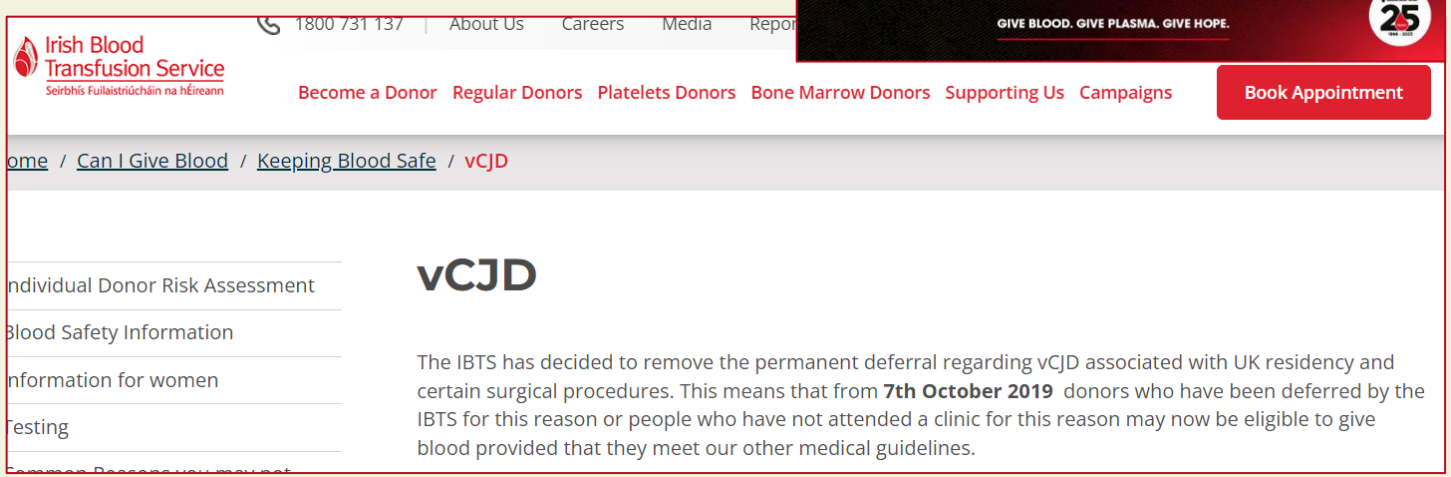
Stephen Thomas[1] | Barnaby Roberts[2] | Dragoslav Domanović[3] | Koen Kramer[4] | Denis Klochkov[5] | Sujan Sivasubramaniyam[6] | Dana Miloslavich[7] | Jean-Philippe Plançon[8] | Françoise Rossi[9] | Dominika Misztela[10] | Lauren Kirkpatrick[11] | Gail Miflin[12] | Janet Birchall[13] | Lorna McLintock[14] | Richard Knight[15]

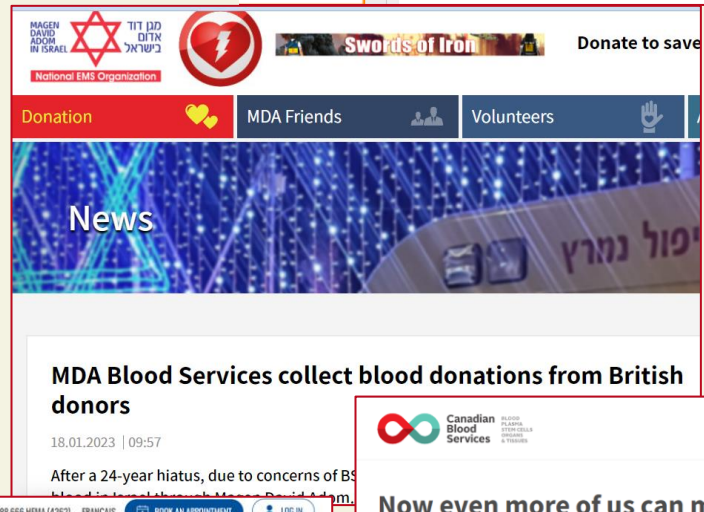
- Less than one death for every 36.4 billion units of UK plasma
- One possible death from vCJD every 33,000 years

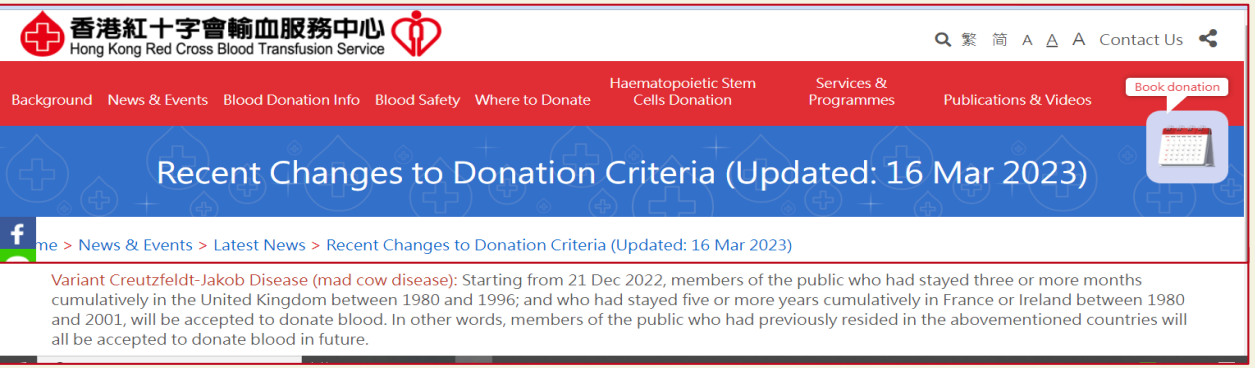

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Guidance for Industry
MAY 2022

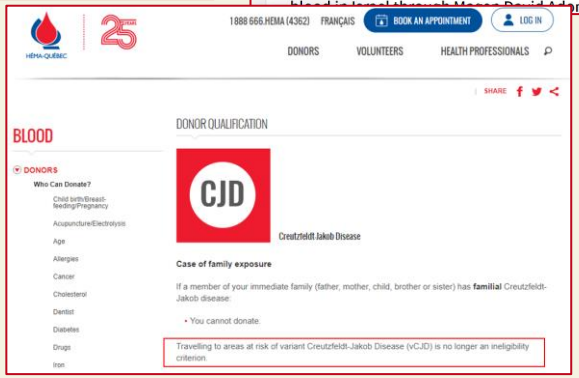

NZBLOOD
The madness is over!
The 'mad cow' blood donation rule in NZ has changed.
GIVE BLOOD. GIVE PLASMA. GIVE HOPE.


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The IBTS has decided to remove the permanent deferral regarding vCJD associated with UK residency and certain surgical procedures. This means that from 7th October 2019 donors who have been deferred by the IBTS for this reason or people who have not attended a clinic for this reason may now be eligible to give blood provided that they meet our other medical guidelines.

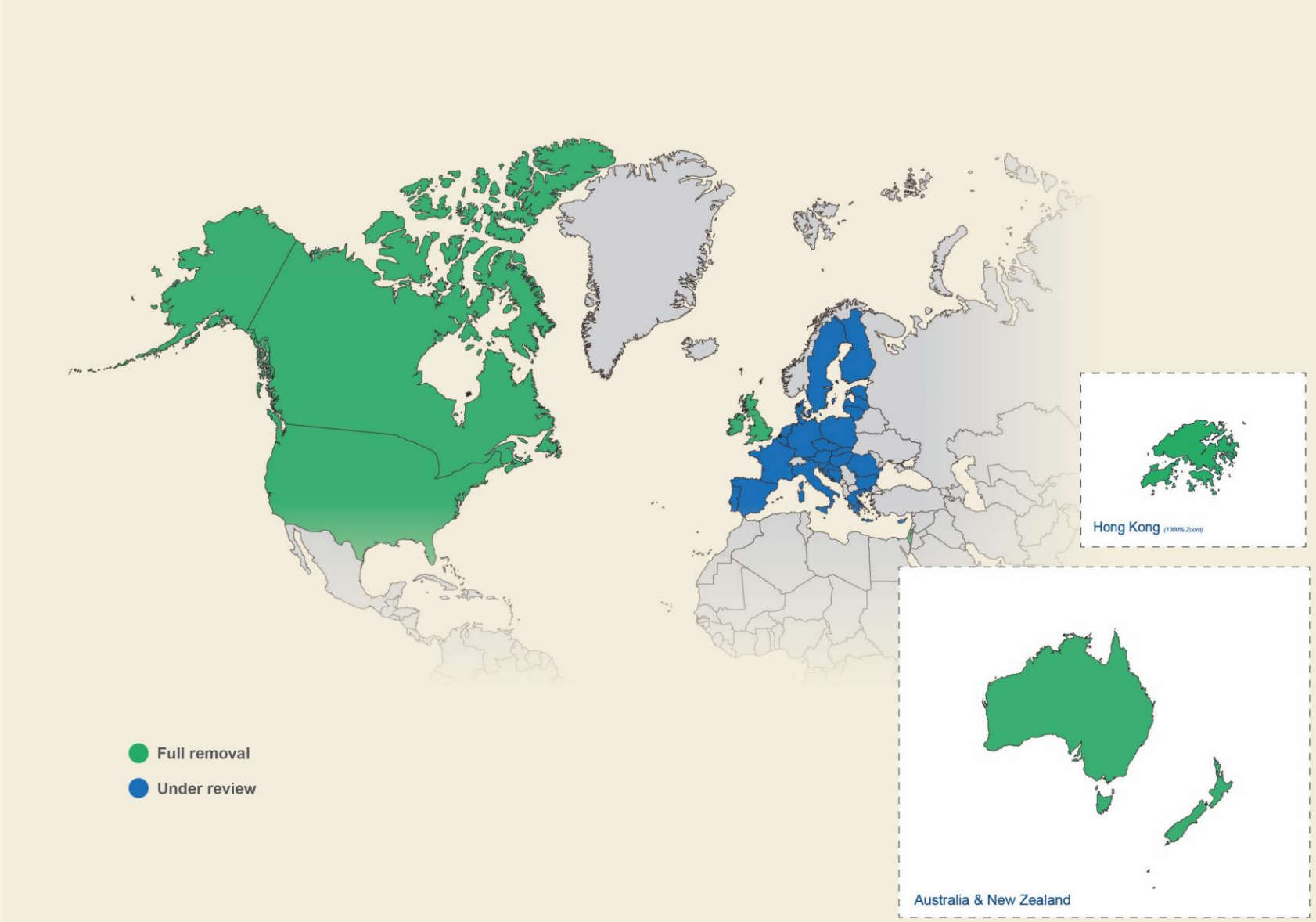

MAGEN DAVID ADOM IN ISRAEL
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News
MDA Blood Services collect blood donations from British donors
18.01.2023 | 09:57
After a 24-year hiatus, due to concerns of BS


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Recent Changes to Donation Criteria (Updated: 16 Mar 2023)
me > News & Events > Latest News > Recent Changes to Donation Criteria (Updated: 16 Mar 2023)
Variant Creutzfeldt-Jakob Disease (mad cow disease): Starting from 21 Dec 2022, members of the public who had stayed three or more months cumulatively in the United Kingdom between 1980 and 1996; and who had stayed five or more years cumulatively in France or Ireland between 1980 and 2001, will be accepted to donate blood. In other words, members of the public who had previously resided in the abovementioned countries will all be accepted to donate blood in future.


1888 666.HEMA (4362)
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Case of family exposure


Canadian Blood Services
Now even more of us can make all the difference.
We've updated donor eligibility criteria related to the 'mad cow' disease outbreak.
Welcome! We've updated our eligibility criteria and are excited to welcome more new donors who wish to make all the difference for patients across Canada.
If you've lived or spent time in the United Kingdom, Republic of Ireland or France during the 'mad cow disease' outbreak of the 1980s and 1990s, you may now be eligible to donate blood, plasma and platelets in Canada.
We can't wait to welcome you to Canada's Lifeline as a donor when you're ready!
You can now book a life saving appointment.
Book now

Increased acceptance of ‘UK donors’



‘UK donor” availability increases blood and plasma supply

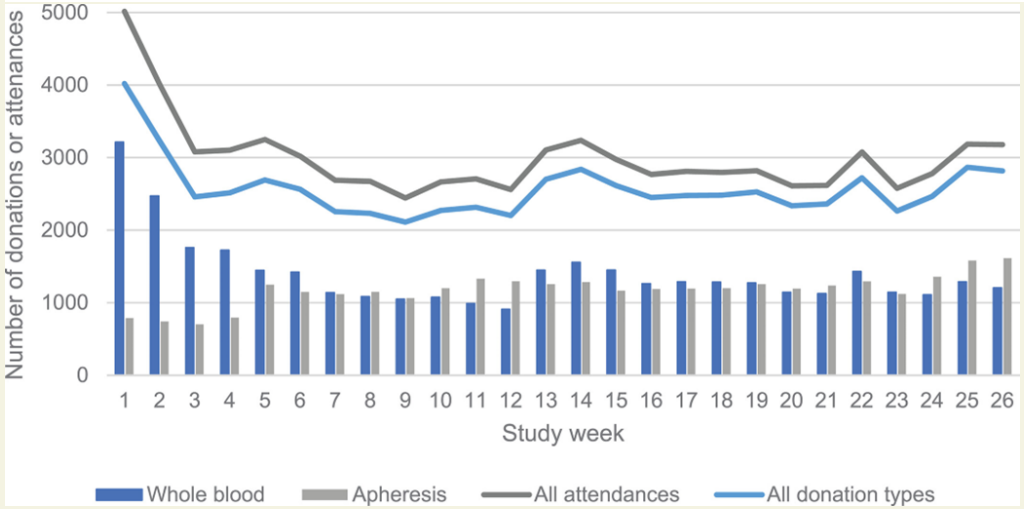
Received: 1 June 2023 | Revised: 25 July 2023 | Accepted: 27 July 2023
DOI: 10.1111/vox.13510

SHORT REPORT

Vox Sanguinis ISBT

Removal of UK-donor deferral for variant Creutzfeldt–Jakob disease: A large donation gain in Australia

Veronica C. Hoad[1] | Clive R. Seed[1] | Philip Kiely[1] | Claire E. Styles[1] | Hamish McManus[2] | Matthew Law[2] | John Kaldor[2] | Iain B. Gosbell[1,3]



32,358 "UK donors" successfully donated 67,914 times in the first 6 months after the change

Vox Sanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion

LETTER TO THE EDITOR

UK donor plasma could have an immediate beneficial effect on the availability of plasma-derived medicinal products in Europe

Stephen Thomas, Venus Ahmed, Barnaby Roberts, Peter Wright, Gail Miflin

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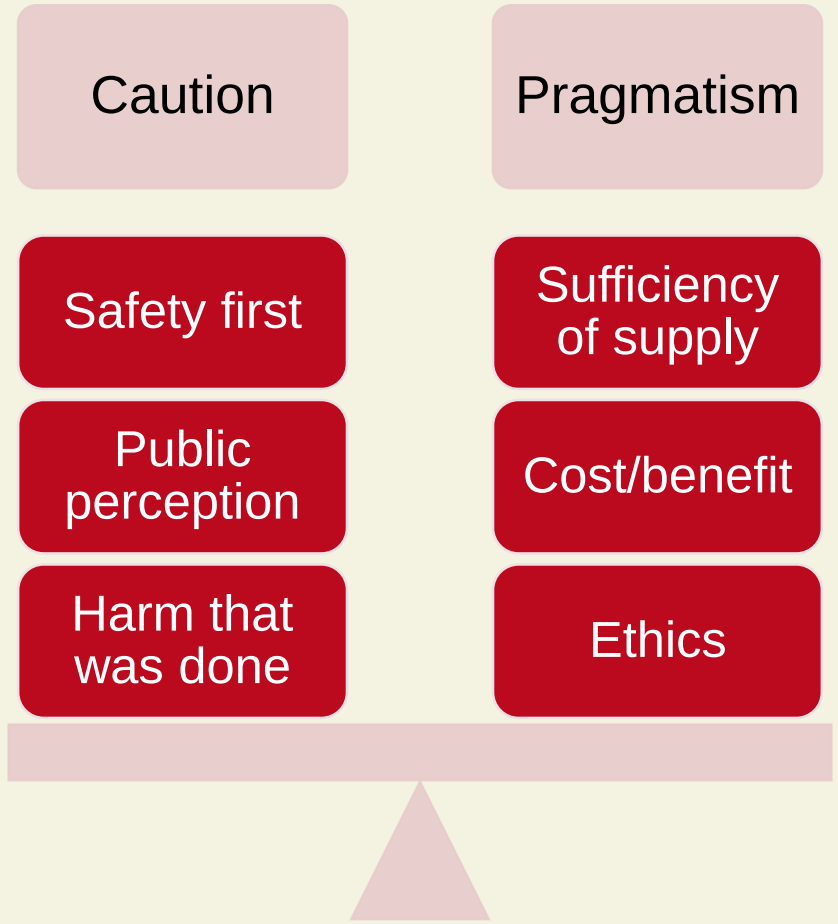
"Europe could immediately benefit from 26,000 [resident] donors who... could contribute at least 12,000 L of recovered plasma per year. "

Is blood a special case?

- Yes, and it will remain so

Is vCJD a special case?

- No, not any more



Thank you

- Prof Richard Knight, University of Edinburgh
- International Plasma Fractionation Association (IPFA)
- Peter Wright, NHSBT Plasma



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