NHS Blood and Transplant

Update on TT vCJD investigations in UK

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NHS Blood and Transplant Colindale

Definite or probable vCJD cases (UK n=177)

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Mean age at death:	30 (range 14-75)
Median age at death:	28
Mean age at onset:	29 (range 12-74)
Median age at onset:	26
Median duration of illness:	14 months (range 6-114)
101 males:	75 females

160 cases tested: all MM at codon129 of the PrP gene

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UK vCJD Cases

- 122 neuropathologically confirmed
- 55 no post mortem

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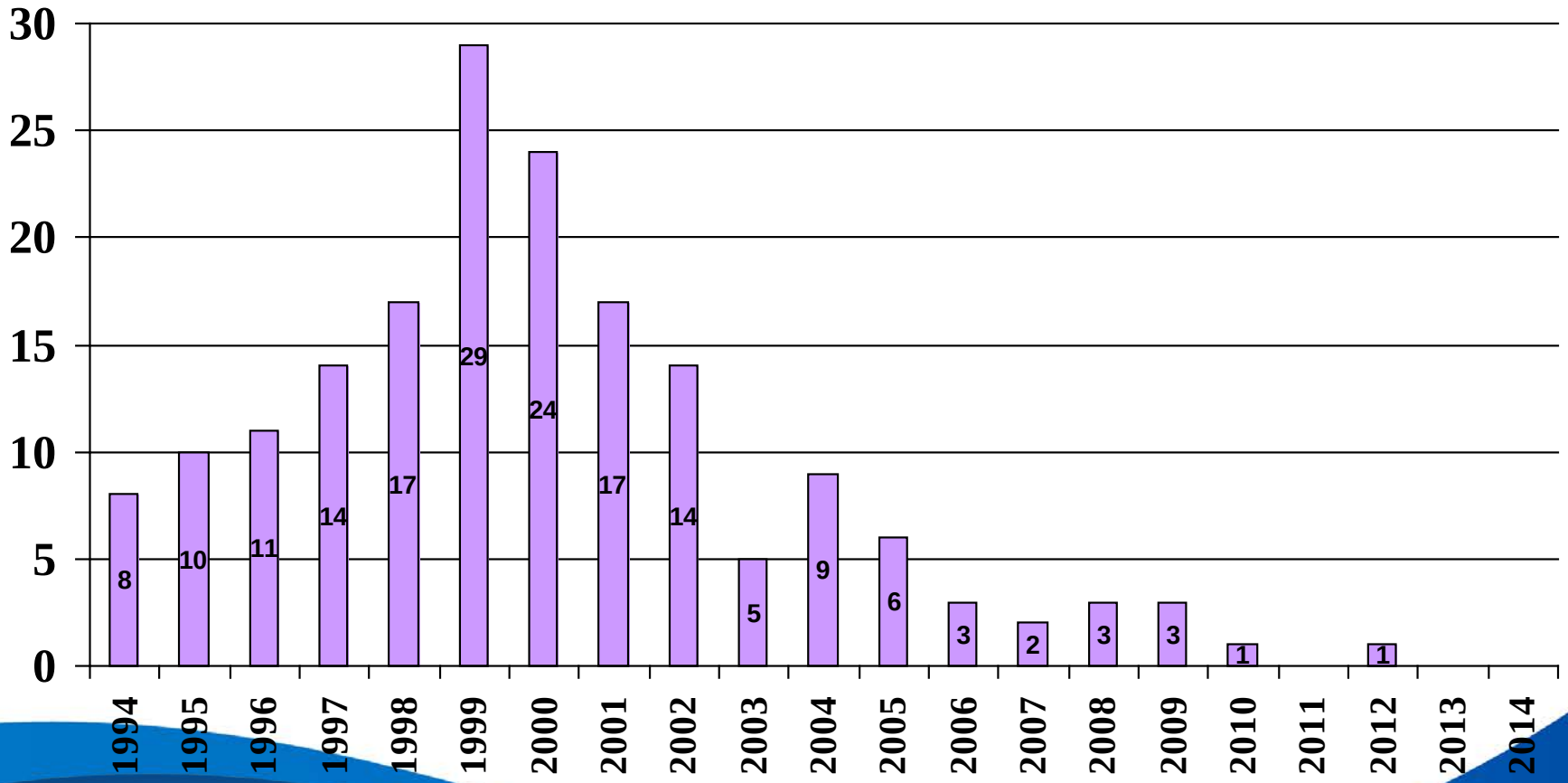
Number of onsets per annum of vCJD in the UK



Number of vCJD cases by 10-year age group

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Age at death	Number of vCJD cases
10-19	22
20-29	78
30-39	52
40-49	9
50-59	11
60-69	3
70+	2
TOTAL	177

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Follow up of donations from individuals with CJD

(Transfusion Medicine Epidemiology Review)

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NHS Blood and Transplant, UK
National CJD Research and Surveillance Unit

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Study outline

- TMER (Transfusion Medicine Epidemiology Review) links databases of UK Blood Services and NCJDRSU
- cases of CJD are actively investigated for history of blood donation/ transfusion
- blood donations are traced through to names of recipient/donors: lookback and traceback
- passive surveillance of those identified: death certificates examined

TMER forward arm: lookback

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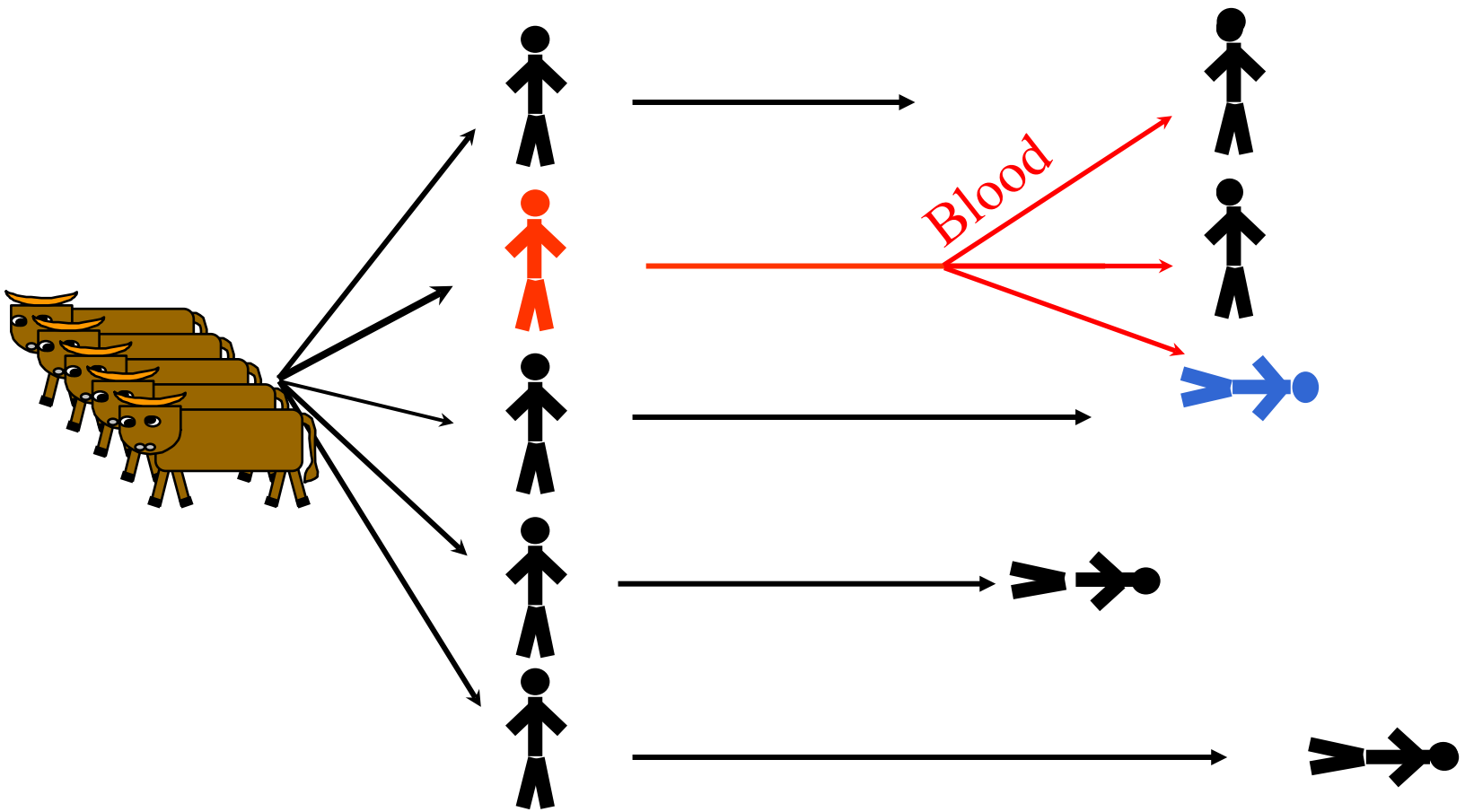
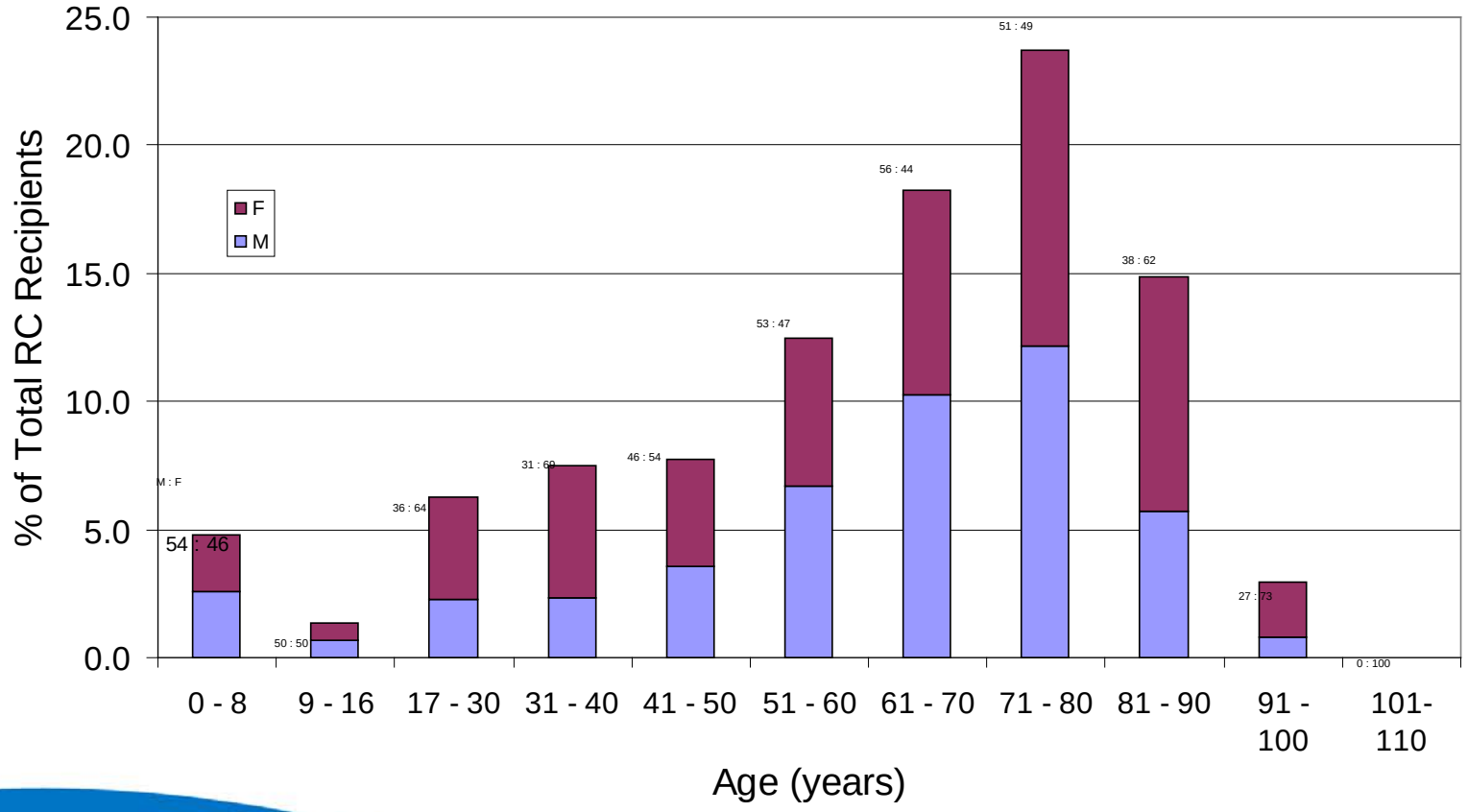


(after M.Busch)

Age distribution for red cell recipients
National Study (24 hospitals) (n=10080)



(Williamson, Murphy, Llewellyn et al, '03)

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vCJD – BLOOD DONORS

total number of vCJD cases in the UK	177
number who were eligible to donate (ie aged ≥ 17)	167
number reported by relatives to have been blood donors	32
number of cases where donor records have been traced	24*
number of cases from whom components were actually issued	18
number of recipients identified from 18 cases where recipient and component information is available	67***

* donor records were traced on four cases where the relatives had reported the case not to be a donor; one of these had donated while the other 3 were registered as donors but never donated

*** some other recipients not identified

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TMER forward arm: lookback recipient outcome

- 34/67 recipients < 5 years survival since transfusion
- 14/67 recipients currently alive
- all living recipients have survived > 10 years

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Decesed recipients with < 5 year survival (n = 34)

- cause of death known; none suggest prion disease
- none had post-mortem/ tissue examination

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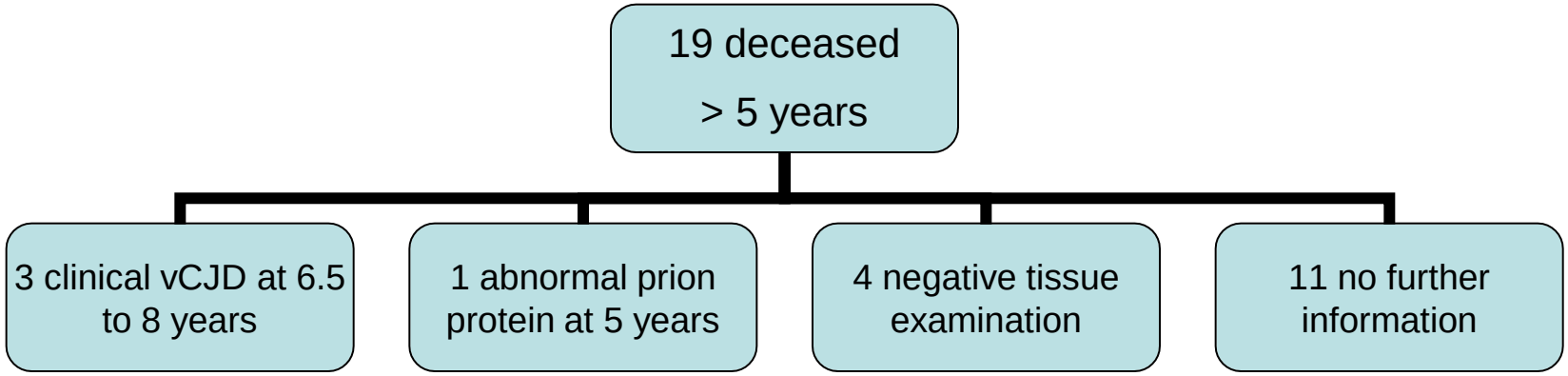
Deceased recipients with > 5 years survival (n =19)



Recipients (n=67) of labile blood components donated by donors who developed vCJD

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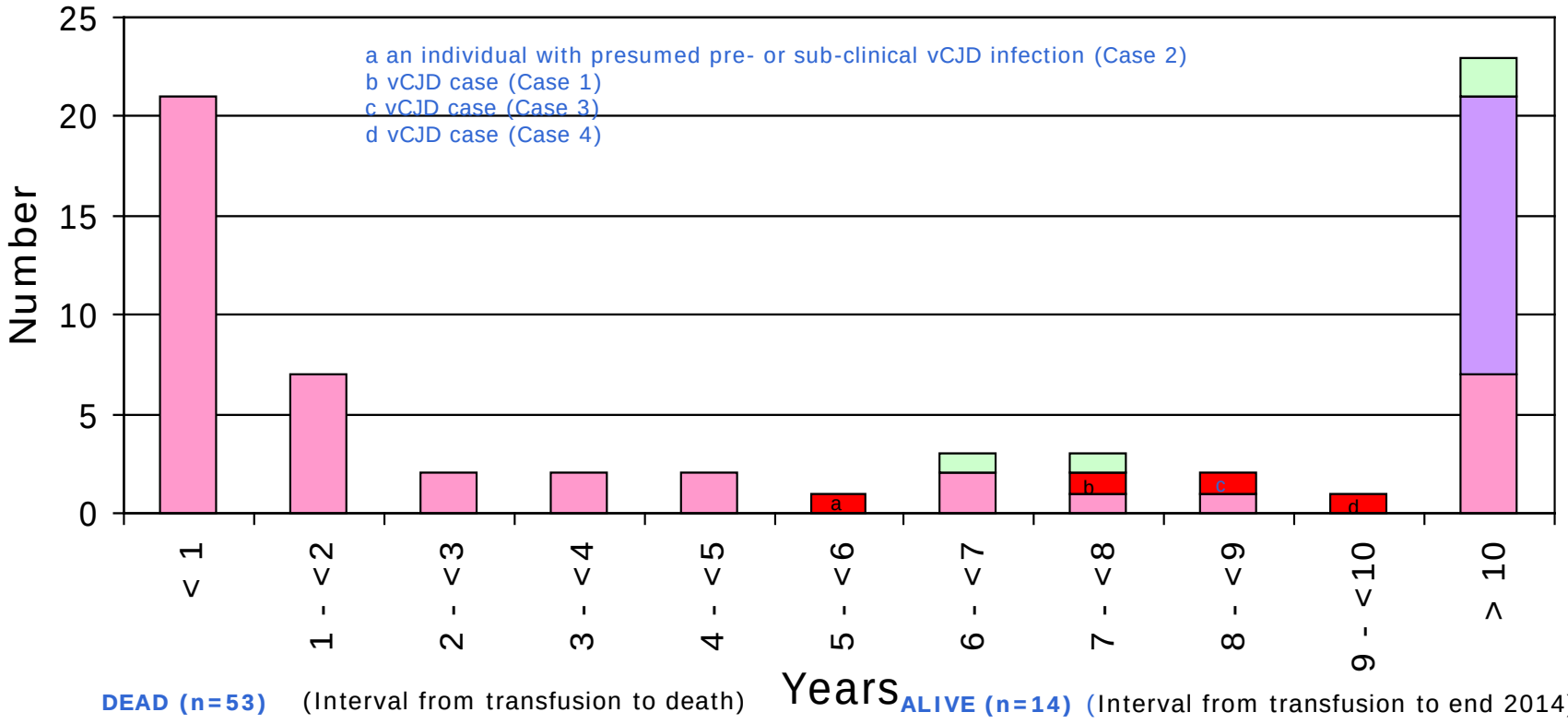

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Living recipients

Recipients of blood from donors who later developed vCJD

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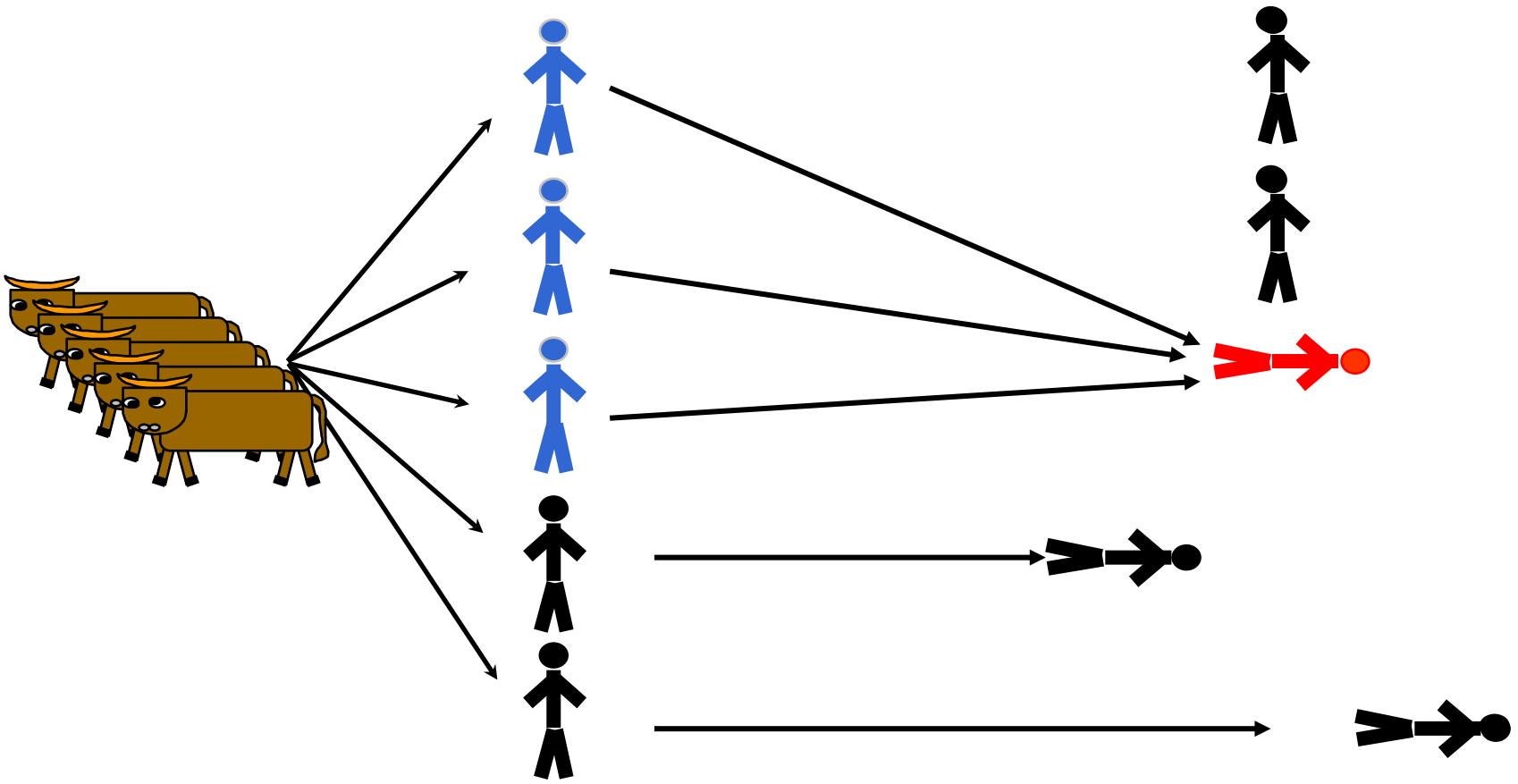
Number of years lived following exposure for recipients currently alive, n=14

Number of years since exposure	Current age group of living patients										Total alive by years since exposure
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	≥90	
0-4											
5-9											
10-14					1	1	2	1			5
15-19				1	2	1		1	2		7
≥ 20						1		1			2

TMER reverse arm: traceback



(after M.Busch)

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Blood Transfusion in vCJD cases: traceback

Total number of vCJD cases in the UK	177[1]
No. of vCJD cases reported to have received a blood transfusion	15[2]
▪ Number not transfused: 1 ▪ Number predating available records: 4 (transfused 1962, 1969, 1971, 1976) ▪ Transfusion records found: 10 (transfused 1982, 1983+1993, 1993, 1994, 1996, 1997, 1997, 1999, 2002)	
Number of donors identified who gave blood to 10 vCJD cases	193
Number of donors already listed on the NCJDSU register as vCJD cases	2[3]

1 Note: recipient with pre-clinical infection (Case 2) is not included in this slide as this patient did not have a diagnosis of vCJD.
2 An additional case received a transfusion after onset of symptoms of vCJD and therefore is not included in the table.
3 two donors diagnosed with vCJD, one with one red cell recipient (Case 1 transfused in 1996), the other with two red cell recipients (Cases 3 and 4, both transfused in 1997).

vCJD CASES WHO RECEIVED BLOOD TRANSFUSION(S) IN THE PAST

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Recipient	Transfusion	Number of donor exposures	Interval from transfusion to onset of illness
1	1	38	4 years, 9 months
1	2	65	4 years, 6 months
2	1	2	15 years, 11 months
2	2	3	6 years, 3 months
3	1	4	5 years, 4 months
4	1	5	8 months[1]
5 (Case 1)	1	5[2]	6 years, 6 months
6 (Case 3)	1	56[2]	7 years, 10 months
7	1	2	13 years, 11 months
8	1	4	16 years, 9 months
9 (Case 4)	1	21[2]	8 years, 4 months
9 (Case 4)	2	2	7 years, 8 months
10	1	2	5 years, 11 months

[1]timing of clinical illness excludes blood transfusion as the source of infection in one case.
[2]one donor developed vCJD.

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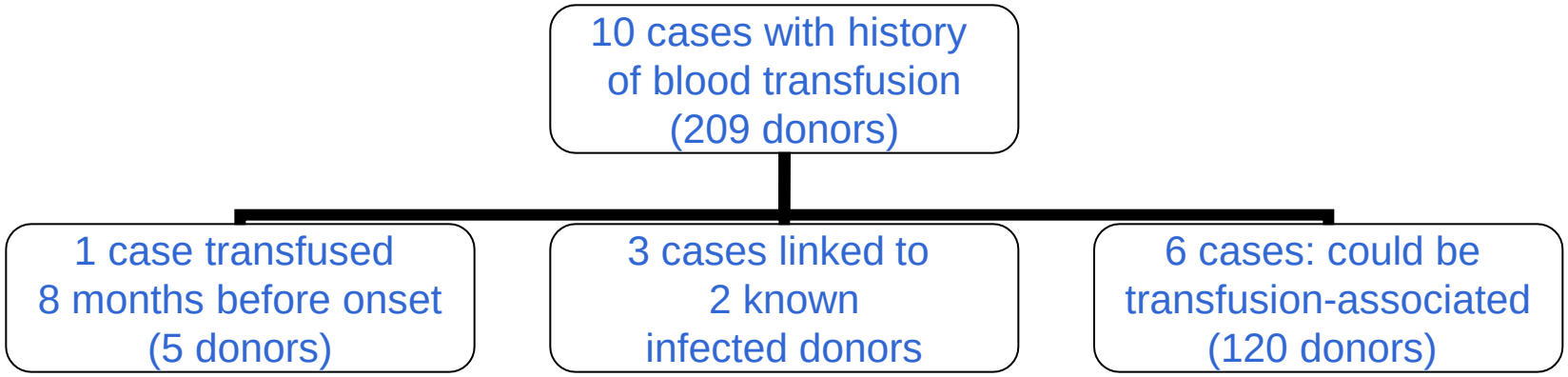
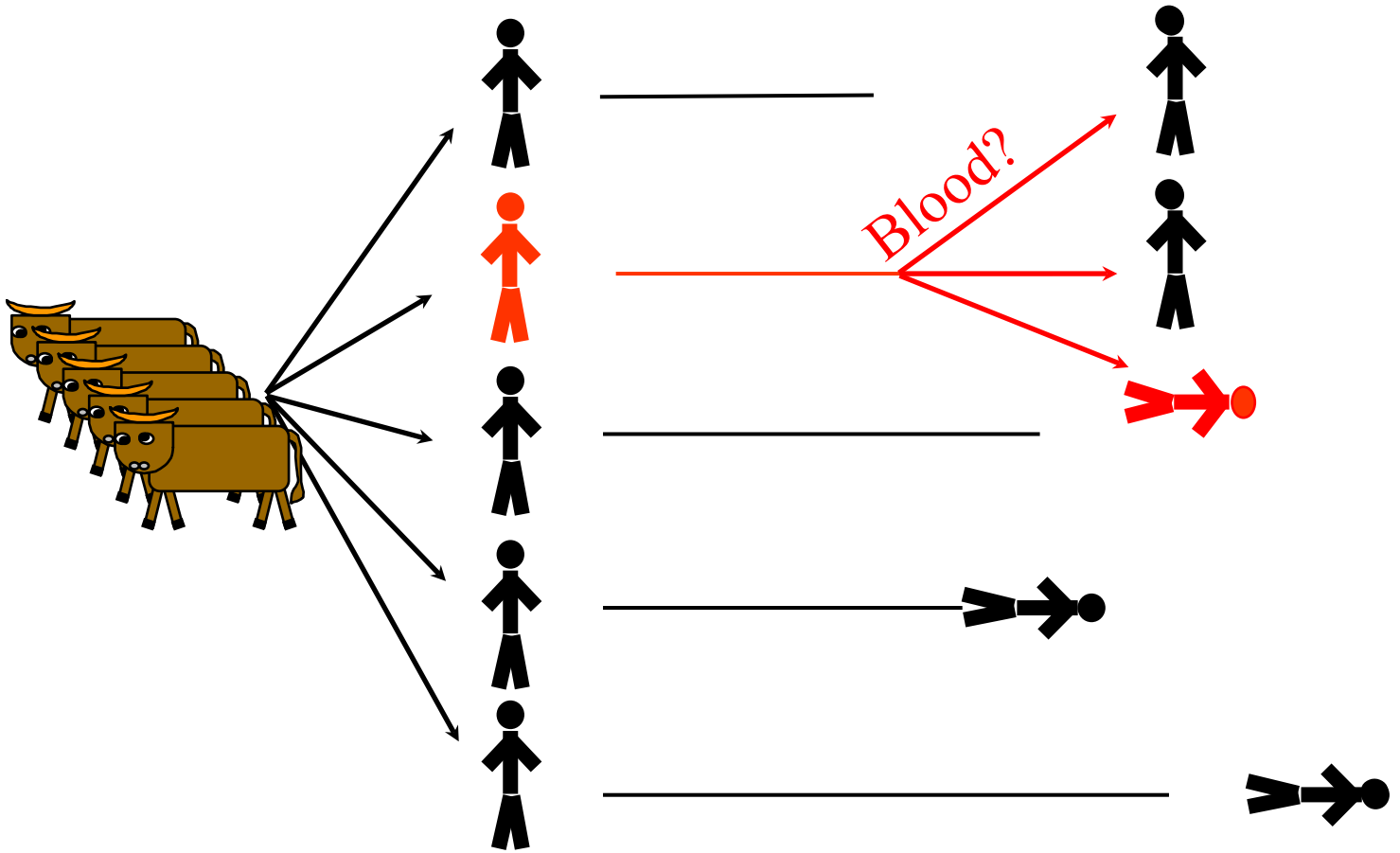
vCJD in transfusion recipients



TMER reverse arm: case 1



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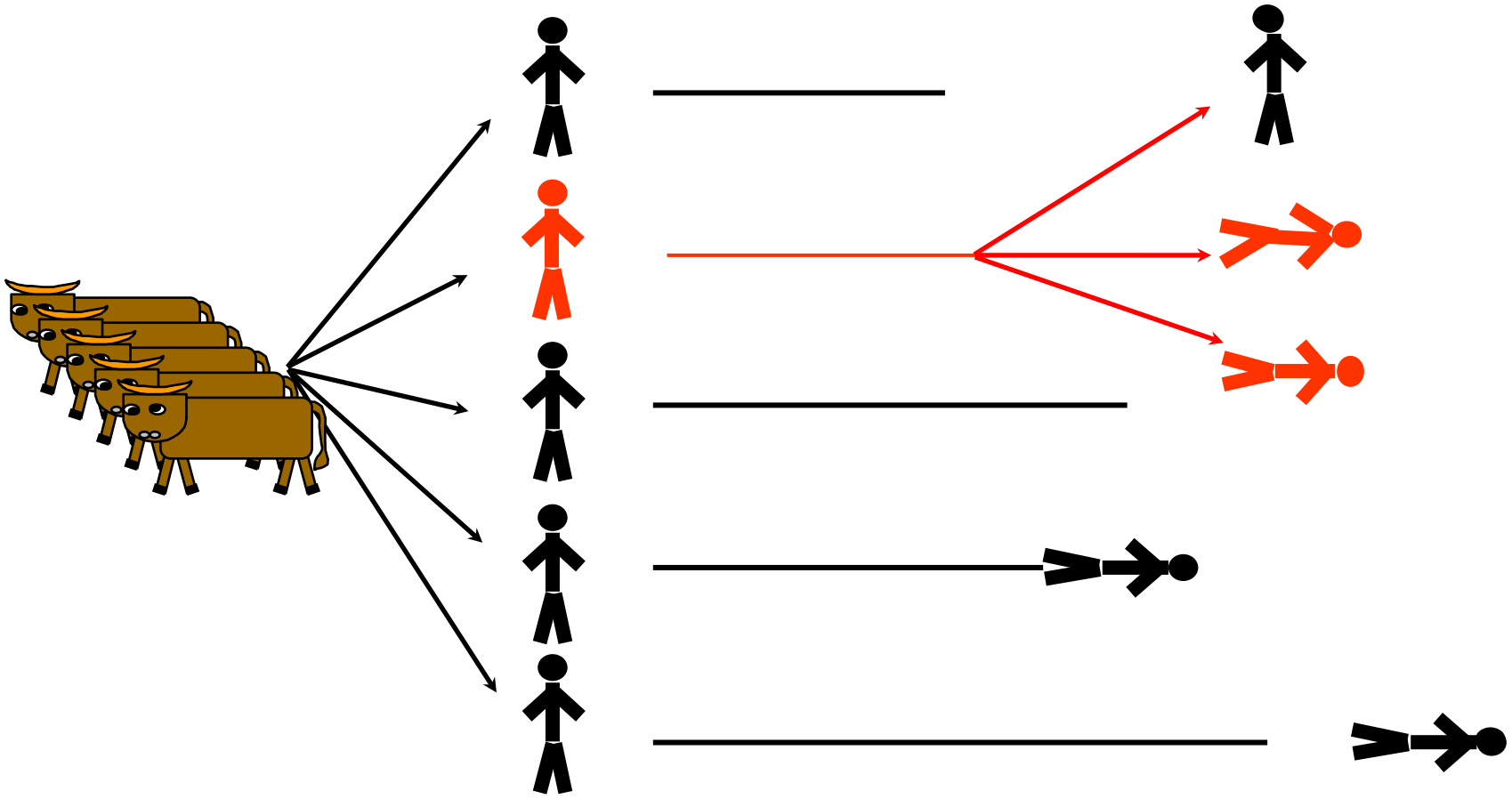
TMER Reverse arm: cases 3 and 4



BSE | vCJD infection | incubation (10-20 years) | death

(after M Busch)

DONOR TO CASES 3 AND 4 AND OTHER DONATIONS MADE

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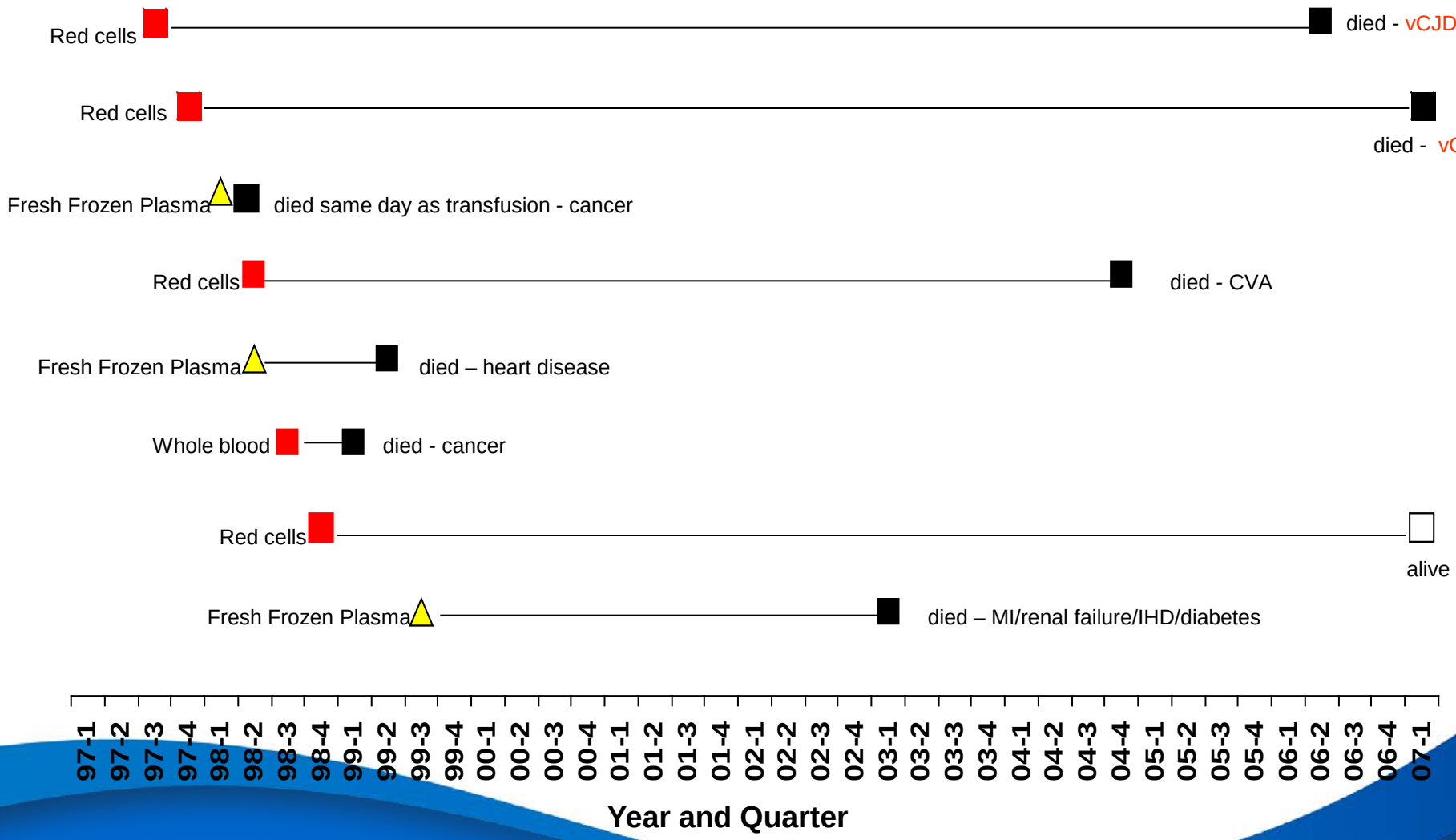

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TMER reverse arm

- 209 donor exposures, 193 identified donors traced of whom 2, already known to have developed vCJD, donated to 3 recipients
- remaining donors to recipients 5, 6, and 9, with already identified infected donor: no further action
- remaining donors in cases with no identified infected donor: notified “at risk of vCJD for public health purposes” and continue under passive surveillance

vCJD CASES WHO RECEIVED BLOOD TRANSFUSION(S) IN THE PAST

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Recipient	Transfusion	Number of donor exposures	Interval from transfusion to onset of illness
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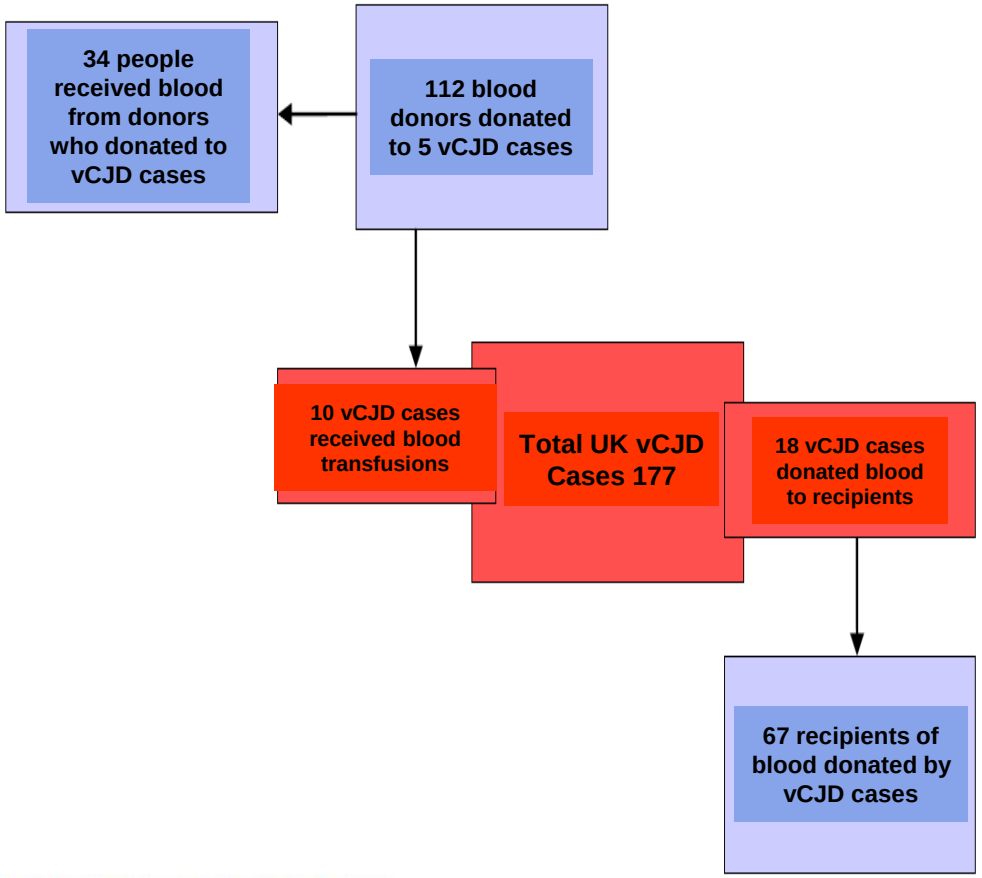
**donors not traced

[1]timing of clinical illness excludes blood transfusion as the source of infection in one case.

[2]one donor developed vCJD.

Patients at increased risk traced to a variant Creutzfeldt-Jakob disease (vCJD) case through blood donations.
Data source: Transfusion Medicine Epidemiology Review (TMER) study.



Journal of Hospital Infection 88 (2014) 22–27

Public Health England

Enhanced surveillance of people at increased risk of Creutzfeldt-Jakob Disease
Biannual Report, February 2015

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Summary of groups identified as at increased risk of CJD on which data are collected (Data correct as at 31st December 2014)

'At risk' Group	Identified as 'at risk'	Number notified as being 'at risk'		Cases	Asymptomatic infections [a]
		All	Alive		
Recipients of blood from donors who later developed vCJD	67	27	14	3	1
Blood donors to individuals who later developed vCJD	112	108	104	0	0
Other recipients of blood components from these donors (reverse risk recipients)	34	32[b]	18	0	0
Plasma product recipients (non-bleeding disorders) who received UK sourced plasma products 1980-2001 [c]	2	2	2	0	0
Certain surgical contacts of patients diagnosed with CJD	196	163 [d]	139[e]	0	0
Highly transfused recipients [f]	3	3	3	0	0

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Follow-up surveillance is conducted by the CJD team at Public Health England, based on data provided by the TMER

P-447

Ten years on–follow up of cohorts with an increased risk of variant CJD through donating or receiving blood

Poster prepared by Katy Sinka and Marta Checchi of the CJD team at PHE

Variant CJD and Blood Transfusion: are there additional cases?

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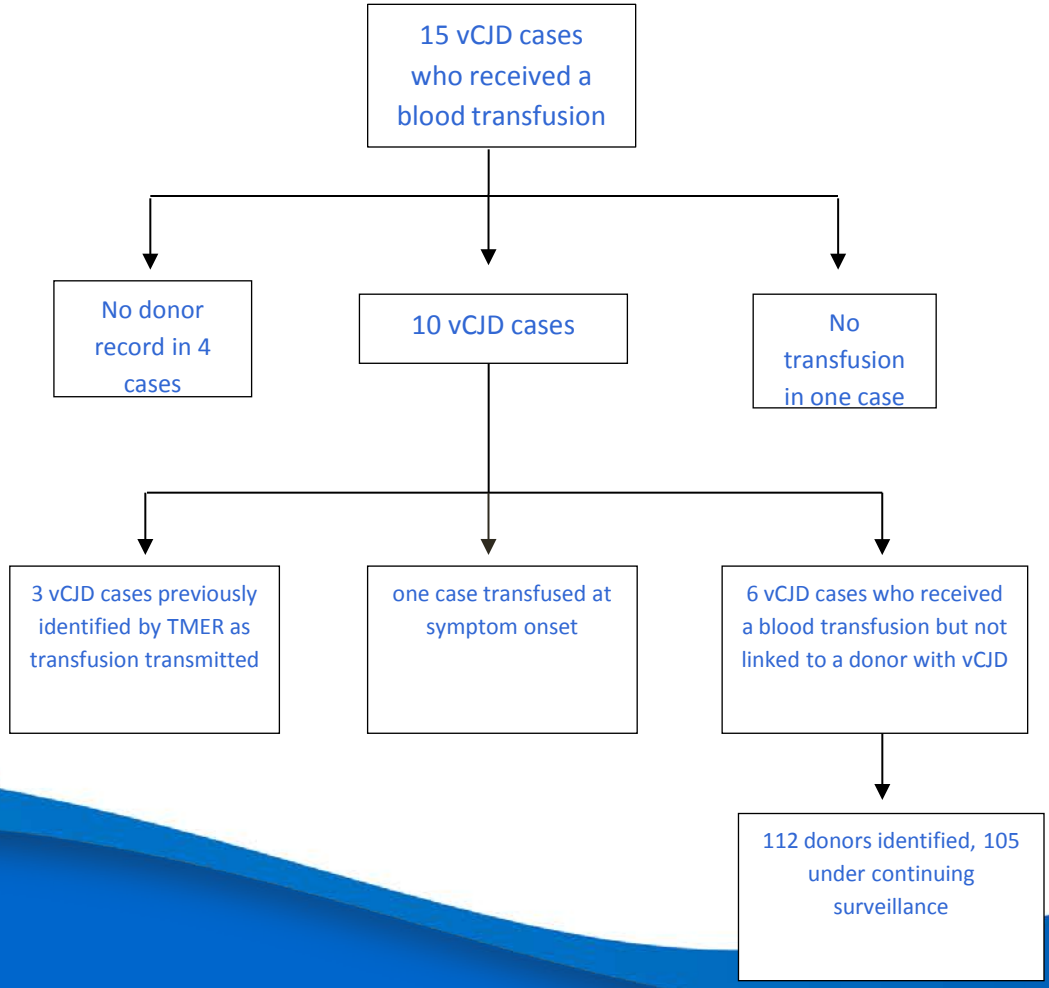
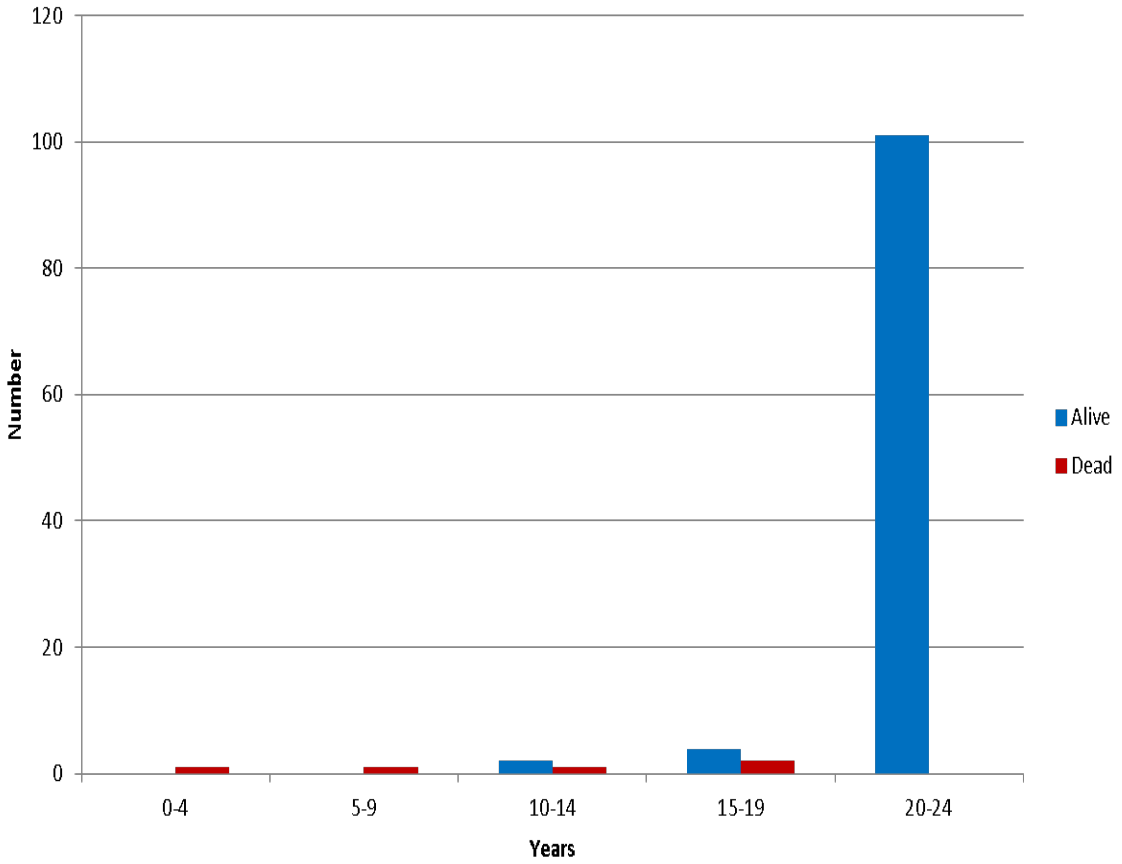
LRR Davidson, CA Llewelyn, JM Mackenzie, PE Hewitt, RG Will: Vox Sanguinis 2014 107 220-225

National CJD Research and Surveillance Unit and NHS Blood and Transplant



Donor survival from transfusion in index case (n=112)



Variant CJD and Blood Transfusion: are there additional cases?

LRR Davidson, CA Llewelyn, JM Mackenzie, PE Hewitt, RG Will

Cause of death among 112 donors to the 5 vCJD cases under review

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Year of Death	Interval from transfusion in index case to death in donor	Cause of death in donor
1994	1 year	Injury to abdominal aorta causing haemorrhage Verdict: Death by Misadventure
2001	8 years	Hypertensive heart disease (Coroner's post mortem without inquest)
2006	13 years, 4 months	Pulmonary embolism/Deep vein thrombosis/ ischaemic heart disease (Coroner's post mortem without inquest)
2008	15 years, 2 months	Bronchopneumonia/disseminated sigmoid colon carcinoma, pulmonary embolism
2012	18 years, 8 months	Complications of heart valve surgery

Variant CJD and Blood Transfusion: are there additional cases?

LRR Davidson, CA Llewelyn, JM Mackenzie, PE Hewitt, RG Will

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Age at onset in variant CJD cases

- Mean age at onset in **primary** vCJD cases
  28.4 years

- Mean age at onset in **3 transfusion transmitted** cases
  57.6 year

- Mean age at onset in **6 recipients** unlinked to an affected donor **35.5** years

VoxSanguinis

The International Journal of Transfusion Medicine

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Conclusion: In conclusion, it is possible that one or more of the vCJD cases that received a blood transfusion derived from an individual not known to have vCJD were infected by the blood transfusion. However, the evidence for this is weak, and the absence of a past history of transfusion in most cases of vCJD excludes a large number of unrecognised transfusion-transmitted cases.

LRR Davidson *et al*, 2014 107 220-225

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VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
Vox Sanguinis (2015) 108, 432–433

DOI: 10.1111/vox.12241

LETTER

Variant CJD and blood transfusion

J. P. Wallis

Older patients with clinical vCJD are more likely to have been transfused, and the mean age will be higher than the whole cohort. Based on the age-adjusted transfusion prevalence, the mean age of cases that might have received an unlinked prior transfusion is 33.4 years. This compares with the observed figure given by Davidson *et al*. of 35.5 years.

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TMER summary

- TMER has used standard blood transfusion lookback and traceback procedures
- and linked blood service and NCJDRSU records
- to investigate any linkage between donors and recipients with vCJD

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TMER conclusions

- 4 cases of prion transmission by transfusion (3 fatal) have been identified from lookback on transfusions in 1996 – 1999
- no further cases of transfusion-transmissions have been identified through traceback from infected recipients
- continued surveillance will be necessary for many years

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Acknowledgements

Jan MacKenzie
Prof Bob Will
Charlotte Llewelyn

Staff in all four UK blood services and in hospital blood transfusion laboratories

The TMER is funded by the Department of Health

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HEV and interventions: UK perspective

Patricia Hewitt NHS Blood and Transplant

ISBT TTID Working Party June 2015

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NHSBT Hepatitis E study 2012-13

- screened 225,000 blood donations over a 12 month period
- 79 (1 in 2850) donations HEV RNA positive
- overall transmission rate 42%
- all recipients eventually cleared infection

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SaBTO HEV sub-group

- UK-wide, with representation from all 4 UK blood services
- examining options, operational and financial considerations

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HEV and blood donations: options

- no screening
- universal screening
- screening for selected recipients (cf HCMV)

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Donor management?

- follow-up testing before return to donation, if so, when?

2013: 5/37 had low level detectable viraemia at 4 weeks after pick-up

- return to donation after set period, if so, when?

- special considerations for “valuable” component (platelet) donors?

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Donor management: workload

- within NHSBT, extrapolating from previous data, universal HEV screening would yield 386 confirmed positive donations in first year, assuming 2012/13 incidence levels

- this is greater than for all other infections combined: 2014: approx 177 in total

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Outcome?

- report to extraordinary meeting of SaBTO in July 2015
- SaBTO make recommendations to Ministers