ANNEX A: BACKGROUND EVIDENCE AND DATA

A1: Total usage of components

Leaving aside a small historical use of whole blood, the annual provision of components by the four UK blood services is shown in the following Table, sourced from successive annual reports for Serious Hazards of Transfusion[1]:

Table A1: Summary of issues by UK Blood Services 1999–2011

Year	Red Blood Cells	Platelets	FFP	Cryoprecipitate	Totals
1999–2000	2,737,572	249,622	365,547	94,114	**3,446,855**
2000–2001	2,706,307	250,259	374,760	95,456	**3,426,782**
2001–2002	2,679,925	251,451	385,236	88,253	**3,404,865**
2002–2003	2,678,098	251,741	377,381	92,768	**3,399,988**
2003–2004	2,607,410	264,539	372,855	95,417	**3,340,221**
2004–2005	2,428,934	258,528	313,019	102,719	**3,103,200**
2005–2006	2,316,152	259,654	320,852	106,139	**3,002,797**
2006–2007	2,235,638	255,474	306,444	116,672	**2,914,228**
2007–2008	2,174,256	258,419	295,085	117,699	**2,845,459**
2008–2009	2,209,153	266,312	306,740	121,555	**2,903,760**
2010 (calendar)	2,180,781	246,962	350,371	120,311	**2,898,425**
2011 (calendar)	2,162,137	301,628	366,416	126,170	**2,956,351**

These figures refer to units issued rather than transfused, so make no allowance for wastage. All components are sourced from UK donors, with the exception of small proportions of FFP used for recipients born after 1st January 1996 and patients undergoing treatment for TTP, a condition requiring particularly high usage. These supplies are now imported, but the change is too recent to have any bearing on the number of vCJD cases seen to date.

Each unit of red cells or FFP comes from a single donor. Platelets (which also contain significant amounts of plasma) can be sourced from a single donor through a process known as apheresis. Although the majority of units are now produced that way, historically most were produced by pooling four separate donations. Cryoprecipitate also involves pooling of several donations. The potential effects of pooling have been considered in more detailed assessment of the relative vCJD risks associated with alternative ways of procuring platelets.

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[1] Available at http://www.shotuk.org/home/

A2: Distribution of units by age of recipients

The distribution of transfusions to recipients by age is calculated using data from the Epidemiology and Survival of Transfusion Recipients (EASTR) study conducted by NHSBT (Llewelyn, Wells, Amin *et al*, 2009; Wells, Llewelyn, Casbard *et al*, 2009). This follows up recipients of transfusion during a 12-month study period in 2001-2 and is the only national survey of transfusion recipients in England and North Wales (i.e. the population served by National Blood Service).

For Red Blood Cells, for example, data show that approximately 65,830 patients were transfused during one year in 29 representative NHS hospitals (stratified into 14 large, 9 medium and 6 small according to red cell usage). Appropriately weighted and scaled up, this suggests that approximately 433,000 patients were transfused with 2,115,650 units of red blood cells in NBS hospitals across England and North Wales in 2001/2002. This would scale up to about 2.5m units for the UK. The distribution of units by recipient age is shown below.

Figure A2: Distribution of RBC units transfused, by age of recipient
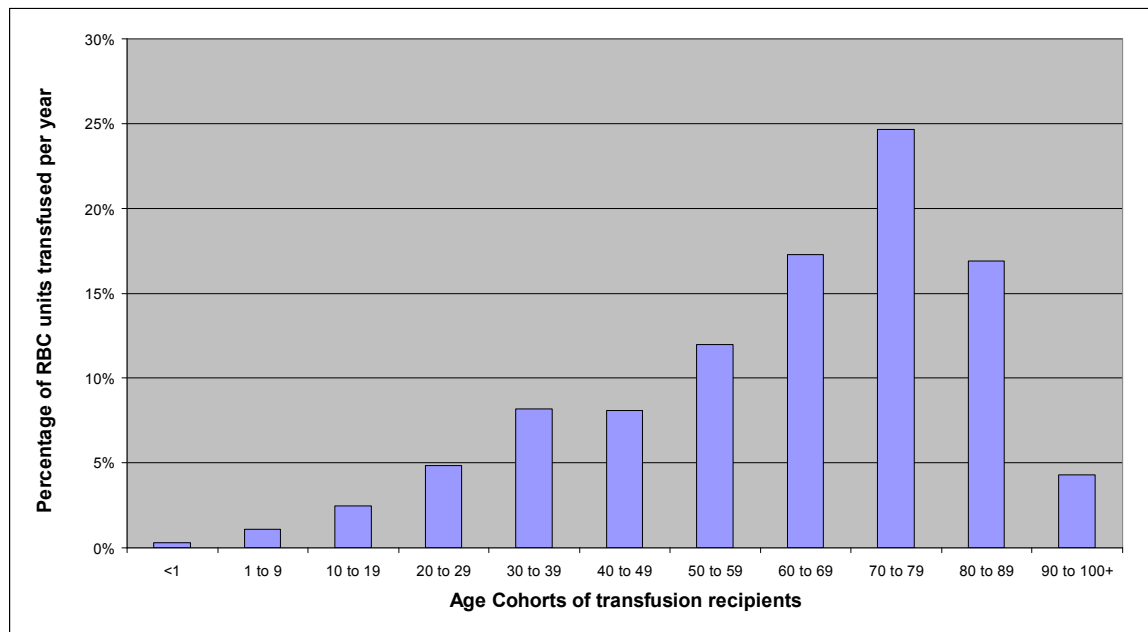
As can be seen, a high proportion of units go to older recipients – e.g. roughly 75% of to recipients aged over 50. Clearly, this is a snapshot for a single year. For the purposes of analysis, we assume that this distribution has not changed significantly.

A3: Post-transfusion survival

Clearly, the number of clinical vCJD cases resulting from blood-borne transmission will have been reduced by the limited survival of many recipients. Two substantial UK studies on survival are available: the "Newcastle" survey of long-term survival after blood transfusion in the North-East (Wallis *et al*, 2004), and the more recent EASTR study already referred to. The latter is a larger study, covering a wider geographical area, whereas the former may be more relevant to transfusions taking place in the late 1990s. The two sets of results are generally similar, with EASTR study suggesting slightly

higher survival rates. Using either study to estimate long-term survival involves extrapolation of the available data (which currently covers up to7 years). In general, however, it is thought that recipients who have survived a few years beyond a transfusion have longer-term life expectancy not much below the norm for their age. This can be estimated from the Interim Life Tables (produced by the Office for National Statistics). Updated results from the EASTR study, following patients up to 10 years after transfusion, will be available later in 2013.

The "Newcastle" study suggests that 47% of all transfused patients were alive after 5 years, and 41% at 7 years. After that, there is about 2.8% mortality per year, reflecting the age distribution of transfusion patients. This would suggest a 10-year survival of 33%. However, the risk of exposure to vCJD rises with the number of units received, and survival is also generally shorter among those requiring multiple units. The better measure for our purposes is therefore to consider the *proportion of units transfused* that go into patients surviving long-term. From the same study, 41% of Red Cell units were transfused to 5-year survivors, with slightly lower figures for FFP and platelets. Applying the same linear mortality rates suggests that at least 28% of Red Cell units were transfused to recipients still alive after 10 years. The equivalent (weighted average) figure for all components was 26.6%.

The vCJD transmission model distinguishes between "acute" and "chronic" recipients. The former receive transfusions on specific occasions (e.g. following surgery or major trauma), whereas the latter typically receive regular, repeated transfusions in response to some long-term medical condition. The pattern of survival for these two groups is somewhat different, with acute patients relatively more likely to die during or immediately after transfusion. In the model, overall post-transfusion survival is calibrated against the empirical data just noted. However, this calibration is somewhat crude, and longer-term survival is subject to significant uncertainties. These become important in scenarios where – as in those presented here – recipients infected with vCJD might develop symptoms only if they survive several decades after infection.

Survival generally varies according to age, as one would expect. For example, estimated 10-year post-transfusion survival rates by age group are shown in Table A3. Rates are the highest for recipients under 40 and decrease steeply with age, to about 1% for recipients aged over 90.

Table A3: Post-transfusion survival by age at transfusion.

Age groups of recipients of RBC	recipients aged under 39 years	40-49 year old recipients	50-59 year old recipients	60-69 year old recipients	70- 99 year old recipients	80- 89 year old recipients	recipients aged over 90 years
Post transfusion survival rates in 10 years	~ 80 %	64%	54%	43%	25%	7%	1%

A4: Transfusion-related vCJD infections and follow-up of recipients

The Transfusion Medicine Epidemiology Review (TMER) study tracks donations from donors subsequently found to have vCJD, and matches these to diagnoses of vCJD in recipients, or to their death from other causes. As noted in the main text, four donor-recipient linkages have been detected. All involved transfusion of non-leucodepleted red cells, which were collected up to 3.5 years prior to onset of symptoms in the donor. Three of these presumed transmissions led to clinical vCJD cases in MM recipients. The fourth recipient, an MV heterozygote, died from unrelated causes, but post mortem examination revealed abnormal prion protein in the spleen and lymph nodes.

The first such match related to a donation given and transfused in 1996: The following table summarises the chronology.

Table A4: Timing of detected vCJD transmissions

	Year of transfusion	**Onset of vCJD in donor**	**Onset of vCJD in recipient**	**Death of recipient**
1996	Case 1			
1997	Case 2 Case 3			
1998				
1999	sub-clinical	Case 1 Case2 Case 3		
2000		sub-clinical		
2001				
2002			Case 1	
2003				Case 1
2004				sub-clinical
2005			Case 2	
2006			Case 3	Case 2
2007				Case 3

More broadly, the TMER study provides information on all detected transfusions of components from donors who developed vCJD. To date, 66 recipients have been identified. These transfusions involved 18 donors in total, and took place between 1982 and 2004. Further detail is provided in the previous paper on scenario generation (Bennett and Daraktchiev, 2011, Annex A). 17 recipients remain alive as of January 2013. 19 recipients survived (or are surviving) for at least 10 years without showing symptoms of vCJD. Information on genotype is available only for a minority, but one might reasonably expect around 8 of these 19 patients to be MM homozygotes. The longest symptom-free survival period (over 25 years) followed a transfusion in 1987. However, even confining attention to those transfused with red cells between 1994 (a plausible timing for onset of substantial infectivity in blood) and the introduction of leucodepletion in 1999, there have so far been four symptom-free survival periods of over 15 years.

ANNEX B: ESTIMATING THE RISK OF vCJD INFECTION FROM PAST RECEIPT OF BLOOD COMPONENTS

(Reproduction of paper to ACDP TSE Risk Assessment Subgroup)
Health Protection Analytical Team
Dept of Health
3rd August 2011

Issue

The scientific uncertainties regarding the possible scale of vCJD transmission via infected blood donations have been well-rehearsed, especially as they affect the potential number of future clinical cases. For risk management purposes, there is also a need to estimate the risk of having been infected by historical exposure to blood and blood products, even where there is no known link to any infected donor. This short note concerns the risk associated with receipt of blood components (including Red Cells, Platelets, FFP and cryoprecipitate). Risk assessment for recipients of UK-sourced plasma products (e.g. Factor VIII) will be discussed in a subsequent note.

Why this is important

Decisions on management of those who may be at increased risk of vCJD infection may depend on assessing the historical risk from potentially-infective blood donations. The CJD Incidents Panel frequently has to make recommendations as to whether people are at sufficiently increased risk to warrant notification, triggering precautions against onward transmission. Clearly, notification is not to be undertaken lightly, and the challenge is to balance possible harm to those notified against the need to minimise any risks of further transmission. In general, the Panel recommends notification unless the risk of infection is estimated to be less than 1%, calculated using precautionary assumptions.

At present, the Panel uses the highly-precautionary assumption that for any recipient of blood components, every donor exposure (in theory, since the start of the BSE outbreak) would have carried a 1 in 4,000 chance of causing vCJD infection. Given the continuing scientific uncertainties, a precautionary approach is certainly warranted. However, there is also a need to ensure that estimates of past risk are consistent with all available evidence, including the small number of clinical vCJD cases presumed to be associated with blood borne transmission seen to date. Overestimating the probability of infection via blood components could have at least two serious and unwelcome consequences:

(a) For someone whose only vCJD "risk factor" has been receipt of blood components, over-estimating the resulting chance of infection could lead to inappropriate notification. This would have personal consequences for the individual, while the concomitant risk management precautions could lead to additional health service costs.

(b) In other circumstances, risk assessment starts with a known clinical case, and considers the relative likelihood of that infection having come from different routes. For example, the individual may have undergone surgery, as well as receiving blood. In this situation, over-estimating the chance of the infection

having come from one route risks *underestimation* of the chance of it having come from another.

The former consideration applies particularly (though not exclusively) to "highly transfused" patients with no links to known vCJD-infected donors, for whom calculated risks are entirely dependent on estimates of historical prevalence and transmissibility. Management of this group has been subject to much debate. Mindful of the dangers of inappropriate notification, and using a threshold of 80 (rather than 40) donor exposures, the Panel has advised that this step should only be taken if patients present for "high risk" surgery. In practice, this has resulted in almost no appropriate notifications.

Proposed approach

Despite the many remaining uncertainties about future transmission risks, we suggest that evidence is now sufficient to justify a new approach. Risks from historical exposure need to be assessed in a way more consistent with case numbers seen to date, while remaining both precautionary and simple to apply.

In particular, any attempt to "calibrate" historical transmission risks against observed case numbers must acknowledge that only a very small proportion of vCJD infections might have led to recognisable clinical cases. The latter may thus be the tip of a much larger "iceberg" of sub-clinical infections.

This can be considered as follows, starting from what is known:

- Approximately 3 million units of components were transfused annually during the 1990s.

- During the following decade, three cases of vCJD occurred in patients who had received blood (non-LD Red Cells) from donors who subsequently developed vCJD: these are presumed to have been blood-borne. Relevant transfusions were in 1996 and 1997(2) and onsets for the recipients in 2002, 2005 and 2006.

- Another four vCJD cases had relevant transfusion histories. Their infections might have been blood-borne, though none of the donors has developed symptoms of vCJD. If so, the relevant transfusions occurred from 1993 onward.

- All these cases were MM-homozygotes. All had incubation periods from transfusion to onset of symptoms of under 10 years (including the four just noted, *if* their infection was caused by transfusion).

Taking a precautionary view, suppose that all these 7 vCJD cases were in fact caused by infective donations. Suppose further that a few clinical cases (or transfusion histories) might have been missed, bringing the hypothetical total to 10. This amounts to an incidence of roughly **1 blood-borne clinical vCJD case per year**, spread over the last decade.

To assess historical rates of infection, the key question is that of the ratio between infections and recognisable cases. How big might the "iceberg" be, relative to the observable "tip" of cases? Given the period that has elapsed since the peak of BSE exposure, and the incubation periods for the observed cases, this question can be posed more precisely:

- ***How many blood borne transmissions of vCJD infection might plausibly lead to 1 clinical case appearing within 10 years of transfusion?***

This will depend on two main factors, one known and one unknown. The known factor is the survival of transfusion recipients. A conservative estimate is that 25% of all units are transfused to patients who survive at least 10 years.

The unknown factor is the proportion of the population susceptible to developing clinical vCJD within 10 years of receiving an infected transfusion. So far, symptomatic patients remain confined to the MM group. Let us therefore suppose that all other genotypes have incubation periods longer than 10 years, by a factor sufficient for no clinical cases to have occurred.

Taken together, these two factors produce a 10:1 ratio of infections to cases: for every 10 infected recipients, only one would be an MM homozygote surviving at least 10 years after transfusion.

However, the large gap between prevalence of vCJD infection in general (evidenced by tissue surveys) and observed case numbers suggests a more precautionary approach, in which we assume that *only 10% of MM homozygotes* would develop recognised symptoms of vCJD following receipt of an infective transfusion, despite this being regarded as a highly-efficient transmission route. The implication is that a very large majority of infections (99 out of every 100) would have so far remained "silent".

Rough consistency with case numbers then permits a worst case in which the historical risk of vCJD infection would have been **1 in 30,000 per donor exposure.**[2]

This is a scenario in which:

- 3,000,000 blood component units were transfused each year
- 100 of these (1 in 30,000) caused infection in recipients
- 25 of these recipients (25%) survived for at least 10 years
- 10 of these surviving patients (40%) were MM homozygotes
- 1 of these surviving MM homozygotes developed clinical symptoms of vCJD

Note that this calibrates transmission to a hypothetical case of 10 blood-borne clinical cases to date, with one such case occurring per hundred historical infections. The comparison with the blood-borne cases *so far detected by TMER* is 3 cases per 1,000 infections. In other words, only 0.3% of blood-borne infections would have been detected. This is illustrated graphically in Figure 1.

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[2]   This could be reached by different combinations of prevalence and transmissibility (e.g. 1 in 30,000 donors being infective, and certain transmission, or 1 in 15,000 and 50% transmission probability). The difference between these is immaterial for present purposes. Given the lower infectivity inputs suggested by recent analysis, pooled production of platelets and cryoprecipitate may have comparatively little impact on transmission risks. It may therefore be unnecessary to distinguish between risks per unit and risks per donor exposure.

Figure 1: Numbers of infections over a 10-year period, related to vCJD cases resulting in the following decade.
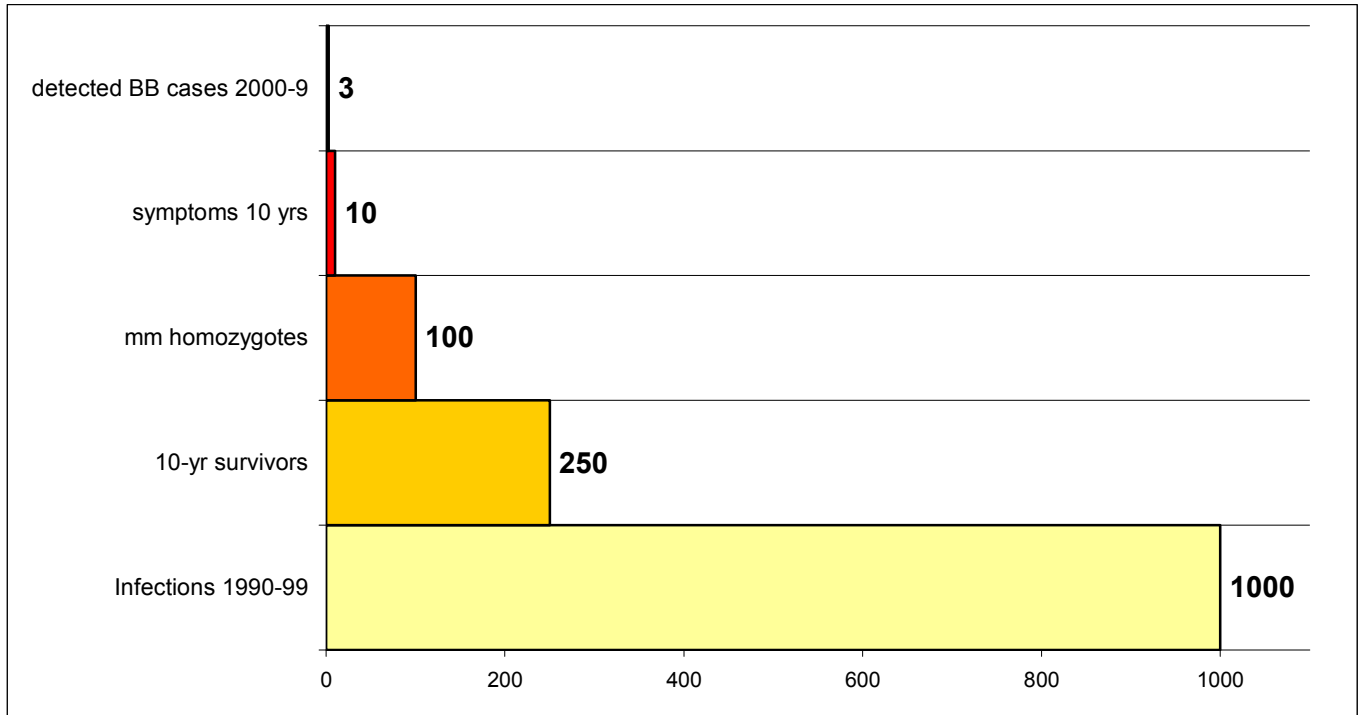
Conclusions

- We suggest that calculations of exposures should count all transfusions from 1990 onward, and continue to treat historical risks per donor exposure as constant.
  - o it appears unlikely that more complex calculations dependent on the age distribution of the donor base are justified as there is now less support for a strong "cohort effect" for historical prevalence of infection – e.g. that it was largely confined to the 1961-85 "Hilton cohort".
  - o other variations may have existed (e.g. delay in onset of infection making earlier donations less risky, while later donations would have been subject to leucodepletion and other precautionary measures) but these are insufficiently known and may tend to cancel each other out.

- Use of this method would produce a substantially smaller estimate of infection risk than that used to date. Nevertheless, the calculation remains precautionary, in assuming:
  - (a) that only a small minority (4%) of secondary vCJD infections amongst recipients surviving at least 10 years would have shown up as recognisable clinical cases, and
  - (b) that more vCJD cases may have been caused by blood-borne infection than the 3 identified so far.

  - If accepted as "appropriately precautionary", a historical risk of vCJD infection of 1 in 30,000 per donor exposure would retain a simple – but arguably more credible – rule of thumb for risk assessment and management purposes.

ANNEX C: PAST AND FUTURE SECONDARY CASES: ILLUSTRATIVE SCENARIOS

C1: Introduction

This annex provides a number of individual scenarios, to illustrate how changes to inputs and assumptions affect the results obtained. For this purpose, we concentrate on the model for red cell transfusion, though similar comments apply to the FFP model.

The scenario used for illustration in the main text (Figure 3, Section 4.3) starts from an assumed prevalence of 1 infected donor in 3,300 for all donors born between 1941 and 1985 (and 1 in 10,000 for those born 1986-95). *For ease of comparison, all scenarios discussed here use these same prevalence inputs*. Changing the assumed prevalence of infection simply changes the model outputs (secondary infections and cases) by the same factor. However, it should be stressed again that the illustrative values chosen are at the low end of the range suggested by the HPA appendix survey.

C2: A non-calibrated scenario

A clear illustration of the problem of model calibration is provided by assigning individually-plausible values to other key parameters. The scenario shown in Figure C1 is generated by assuming:

- Infectious dose per unit of 1 ID prior to leucodepletion, and 0.5 ID after

- Mean delay in onset of infectivity in donors of 3 years (for all genotypes)

- Mean secondary incubation periods of 10 and 20 years for MM and non-MM recipients

Combined with the prevalence estimate already noted, these are by no means "worst case" assumptions for individual parameters. However, the resulting scenario is – fortunately – completely unrealistic. As shown in the top graph, infections via red cell transfusion would have peaked at about 350 per year (before being reduced by leucodepletion in 1999), and would then continue at about 200 per year for well over 20 years. The rate would eventually tail off as more donors came from amongst those born after 1996.

Although many of the infected recipients would die of other causes before developing vCJD, there would still be a very large number of clinical cases, as compared with what has been seen to date. Incidence of cases is shown in the lower graph: these would total **385** to the end of 2012, and **nearly 1400** from the start of 2013 onward.

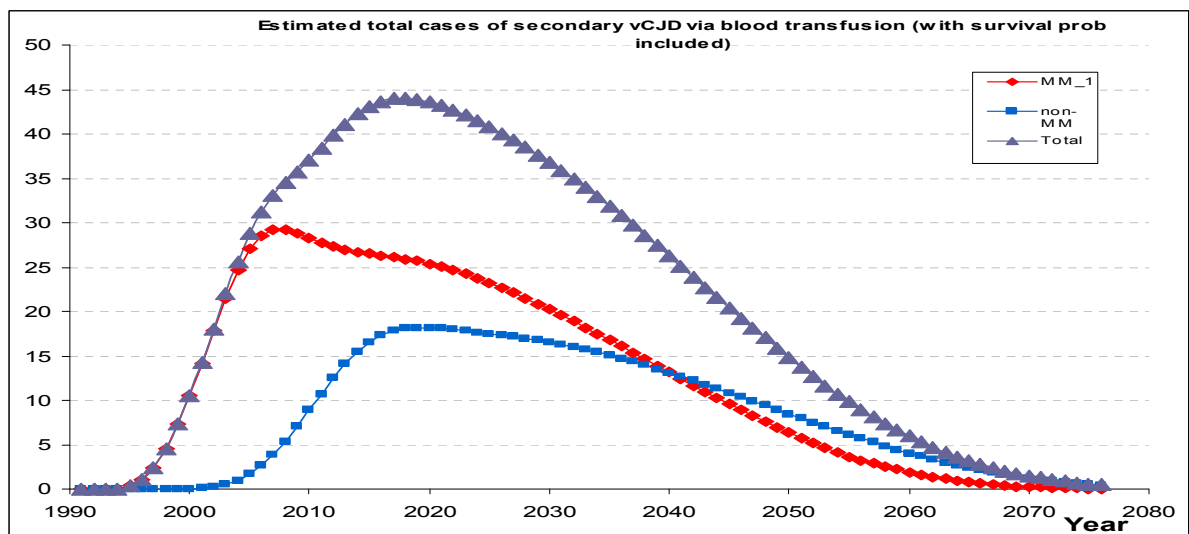Figure C1: Uncalibrated scenario for red cell transmission

(a) Secondary infections, by calendar year
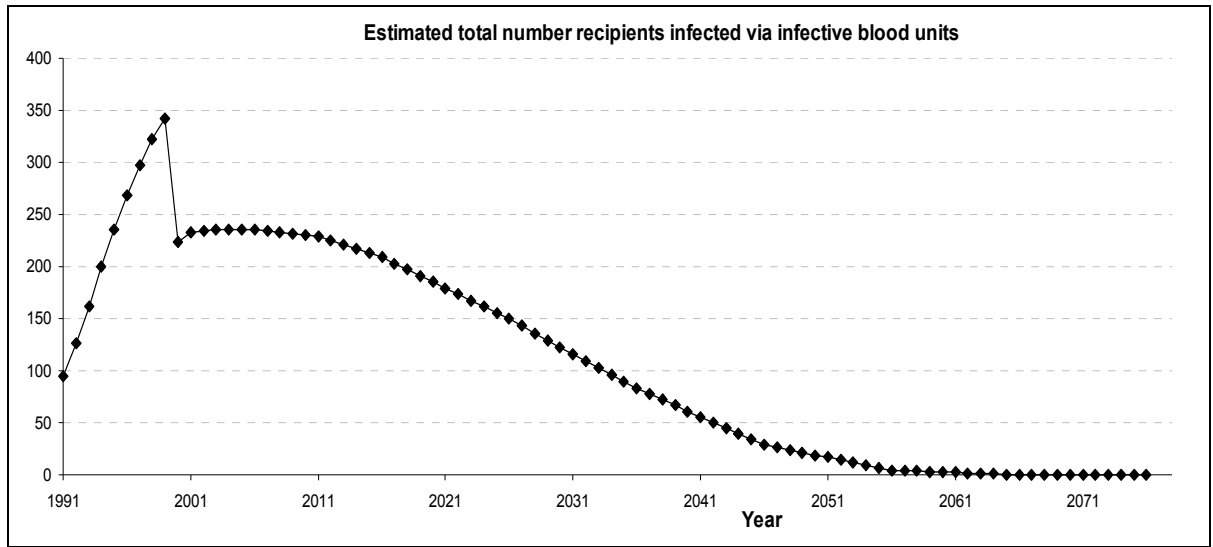
(b) Resulting clinical cases (note change in scale)
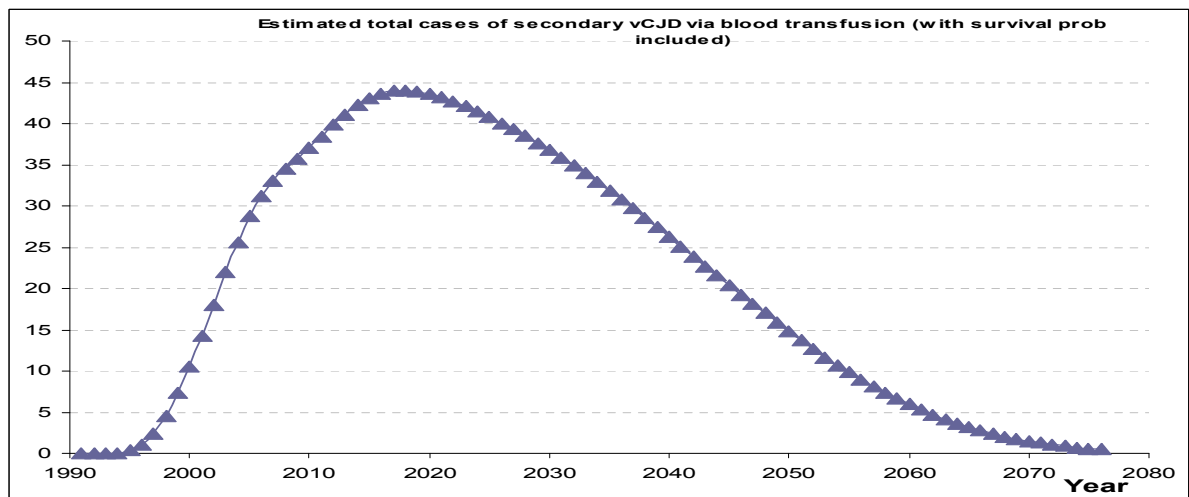
(c) Cases broken down by genotype

C2. Sensitivity analysis

A scenario such as that just set out cannot be regarded as realistic: the number of clinical cases seen to date is too high, arguably by a factor of 100. There are some simple ways of changing individual assumptions to remove this "over-prediction" of cases. For example, we might assume:

- that only 1 patient in 100 is susceptible to infection, or - more plausibly - to development of clinical vCJD

- a much lower prevalence of infective donors (meaning that the results of the appendix survey do not necessarily indicate infectivity in blood).

Another variable with some impact is the onset of infectivity in donated blood. This is of particular interest because it can substantially reduce the expected number of cases seen so far, while having a smaller effect on future case numbers. For example, if we take the previous scenario, but assume a mean delay in onset of 7 years for MMs and 15 years for other genotypes, the projected number of cases to date reduces to **106**, whilst there would still be roughly 1200 from 2013 onward.

Clearly, this would still leave a substantial over-prediction, whilst such a long delay is difficult to reconcile with the results of studies of ovine transmission noted in the main text. Nevertheless, allowing for the *possibility* of a relatively long delay is precautionary, given that this allows for scenarios in which transmission risks might have been increasing. The scenarios considered in the main paper therefore permit a wide range of values.

Other factors, such as the *variability* in timing of infectivity onset, or in the timing of primary infections amongst donors, have only minor effects on model outputs.

C3. Illustrative "calibrated" scenarios
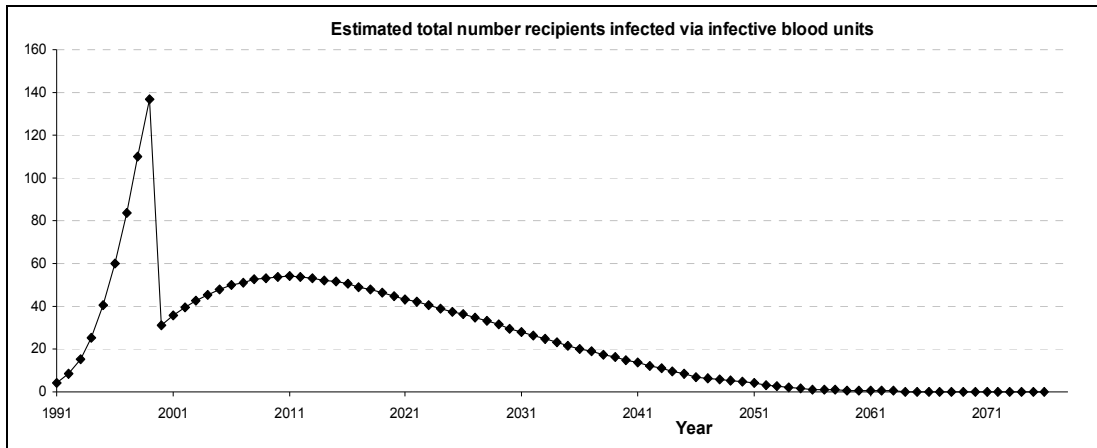
Initial example

Our overall approach to model calibration has been to consider different *combinations* of inputs that can avoid "over-prediction" of existing case numbers, with due allowance for the point that more blood-borne clinical cases might have occurred than have so far been identified: hence the upper limit of 9). The scenario used for illustration in the main text (reproduced in Figure C2) achieves this by assuming (in addition to prevalence near the bottom of the "appendix survey" range):

- *Mean Incubation periods* following blood-borne vCJD infection: 9 years for 10% of MM infections, (designated "MM(1)"); 25 years for other MM infections; 30 years for other genotypes.

- *Mean delay in onset of infectivity in donors:* 7 years for MM donors; 12 years for other genotypes.

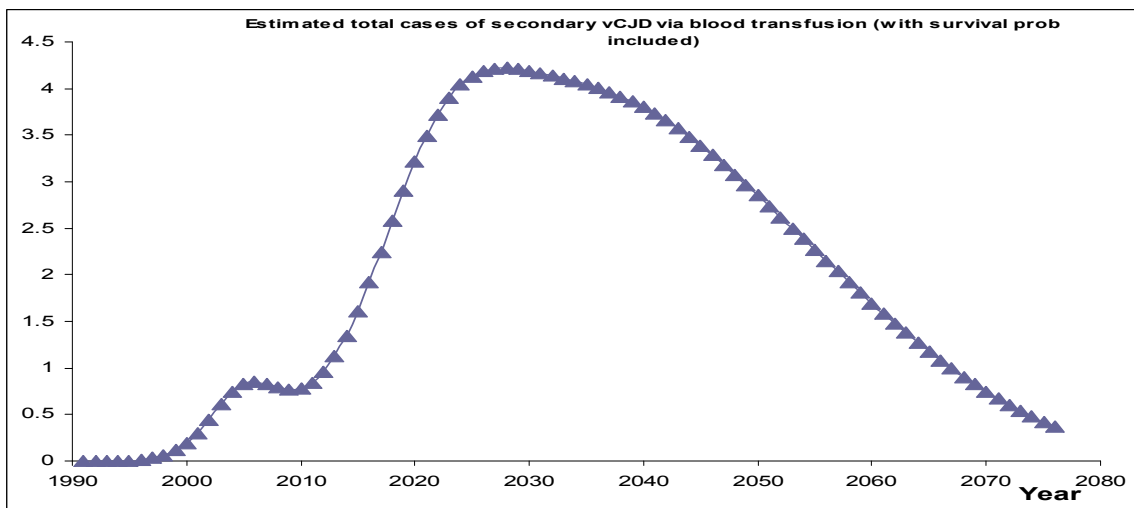- *Per unit infectivity:* 0.7 ID pre-leucodepletion, 0.1 ID after.

This scenario has **9** clinical cases appearing by the end of 2012, and **167** thereafter.

Figure C2: Illustrative scenario for Red Cell transmission (as in main text)
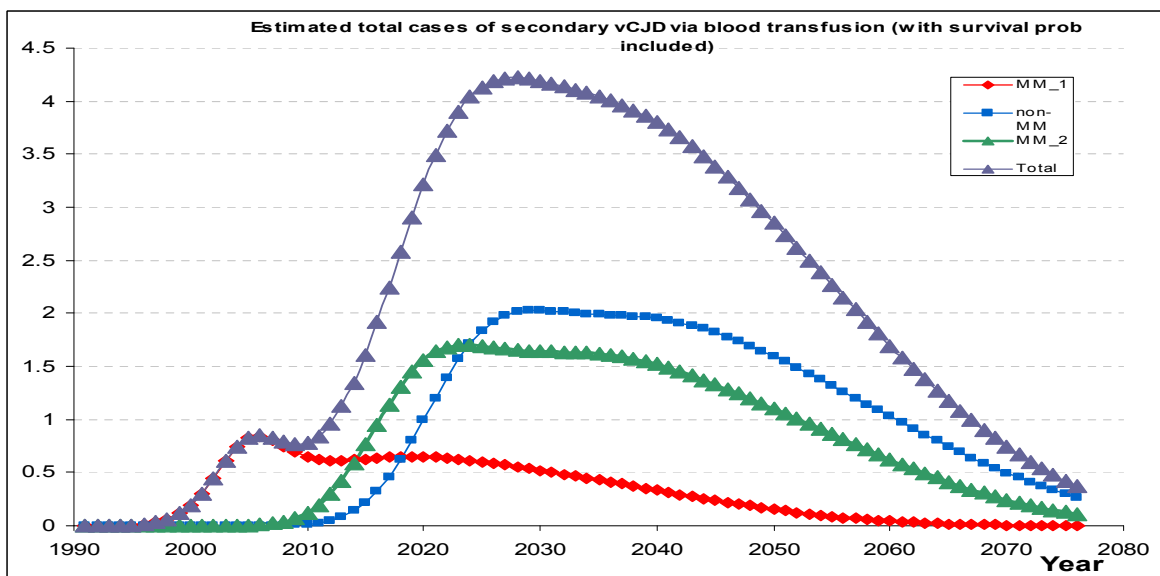
(a) Occurrence of secondary infections, by calendar year

Estimated total number recipients infected via infective blood units

(b) Appearance of clinical cases amongst transfused patients (NB change in scale)

Estimated total cases of secondary vCJD via blood transfusion (with survival prob included)

(c) Breakdown of clinical vCJD cases by patient genotype

Estimated total cases of secondary vCJD via blood transfusion (with survival prob included)

- MM_1
- non-MM
- MM_2
- Total

Limiting susceptibility

The previous scenario takes all recipients to be susceptible to clinical disease, but relatively short incubation periods are confined to a small minority of infected MMs – whether due to differences amongst individual patients, between strains of infection or both. An alternative is to allow limited susceptibility to clinical disease, following infections of all genotypes. For example, Figure C3 shows a scenario based on similar inputs to C2, except that only 10% of recipients ever develop clinical disease. For infections that *do* lead to disease, mean incubation periods are 10 and 25yrs for MMs and non-MMs respectively. This scenario has **8** clinical cases appearing by the end of 2012, but only **30** thereafter - as compared with 167 in the previous example.

Figure C3: Scenario with limited susceptibility across genotypes

(a) Infections – as Figure C2

(b) Appearance of clinical cases
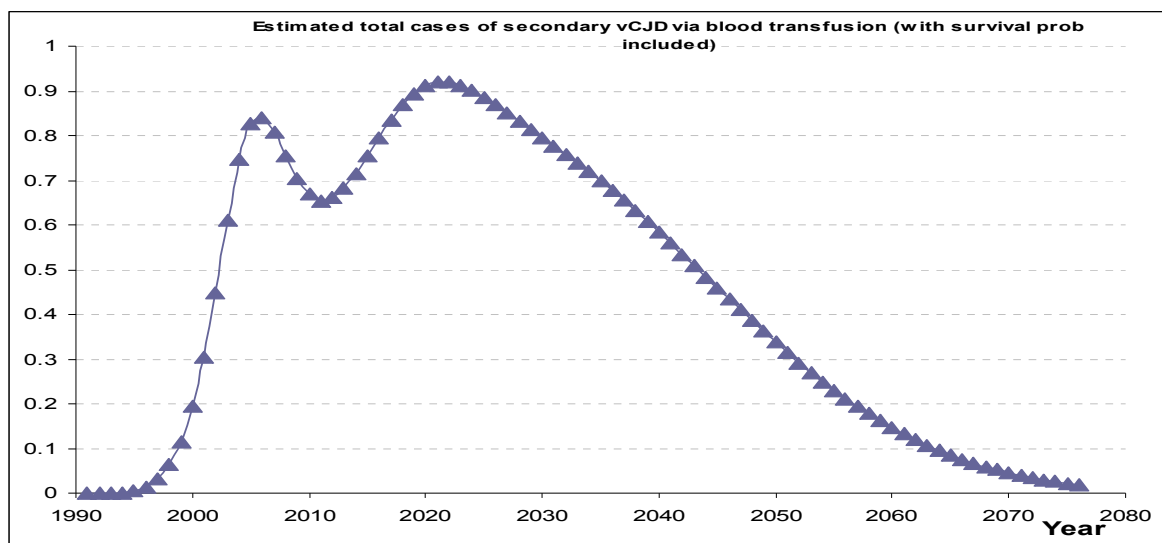
(c) Breakdown of cases by genotype
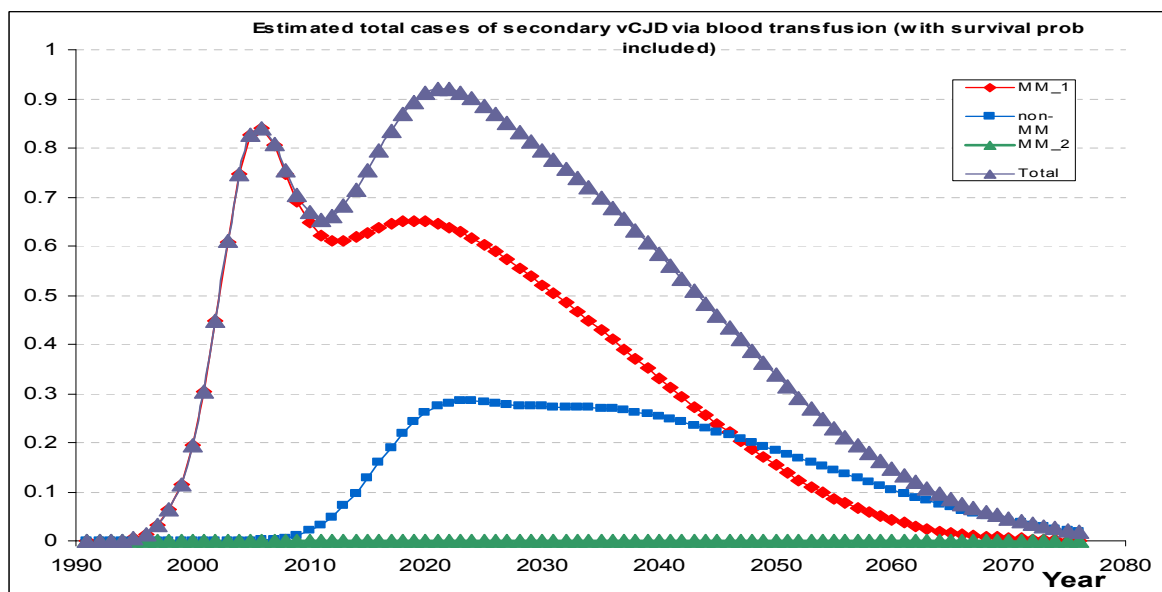
Limited susceptibility combined with bimodal incubation periods

The contrast between the last two scenarios is interesting, and demonstrates the potential impact (in the first) of a bimodal distribution of incubation periods within a given (MM) Codon-129 genotype.

The scenarios in the main paper use *either* of these hypotheses (bimodal incubation periods or limited susceptibility), rather than both. However, it is noteworthy that allowing both these factors to vary makes it much easier to produce "calibrated" scenarios. For example, Figure C3 shows a scenario with the same background assumptions as before, except that:

- development of clinical symptoms is confined to 30% of MMs and 10% of other genotypes

- for those infections that would lead to clinical vCJD, mean incubation periods are split thus:

    o 6 years for 10% of MM infections

    o 25 years for infections of other MMs

    o 30 years for infections of other genotypes

This has **5** clinical cases up to the end of 2012, and **38** from 2013 onward. This is arguably the most "realistic" example considered so far. Calibration could still be achieved with a higher prevalence of infected donors, and/or with less benefit from leucodepletion.

Figure C3: Limited susceptibility and bi-modal MM incubation periods

Appearance of clinical cases, by genotype
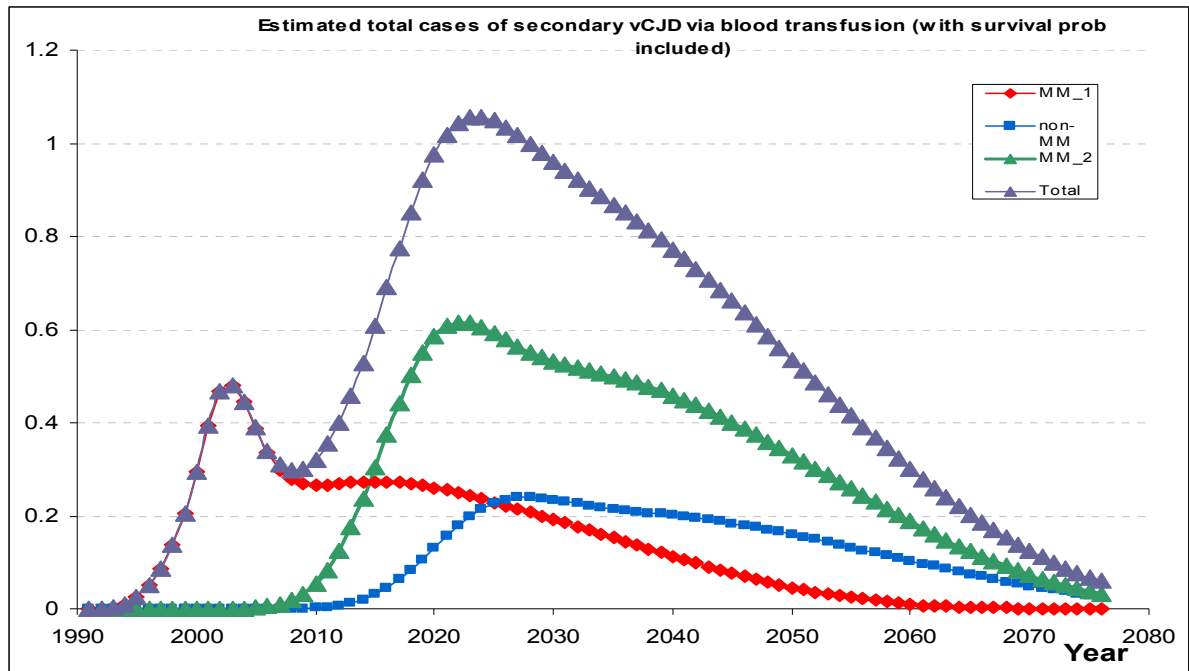
The "best case"

Finally, it is worth noting that there are scenarios compatible with what has been seen so far by way of blood-borne clinical cases, in which there would be very few such cases in future, if any.

For example, if we were to assume that to clinical disease following blood-borne infection would be confined to a small minority of MM homozygotes (say 4%), *and* that leucodepletion has reduced the risk of transmission to negligible proportions, then the following scenario is generated.

Figure C4: "Best case" scenario for future vCJD cases
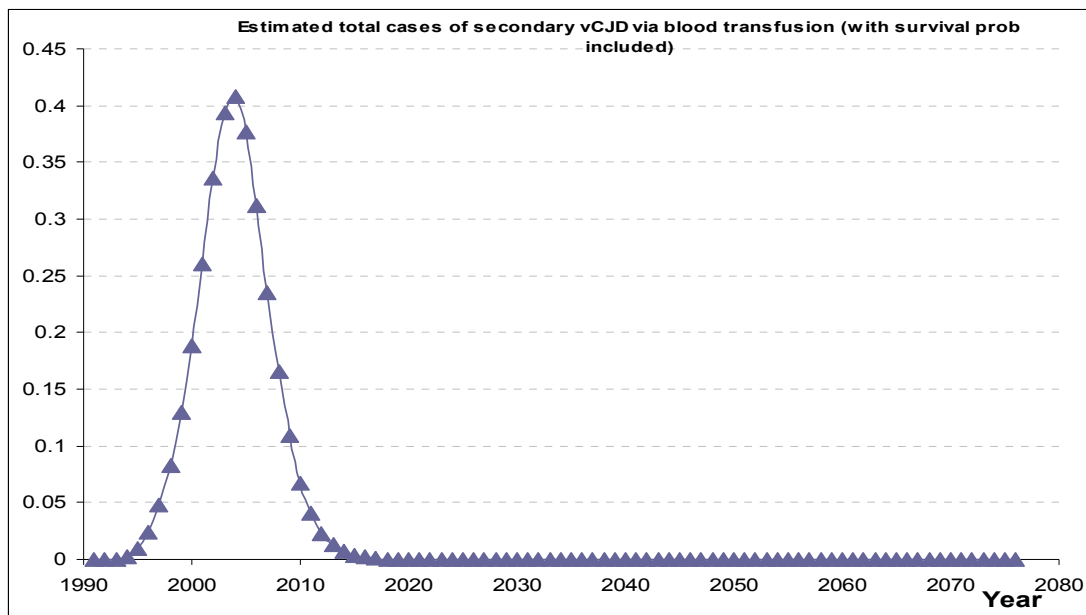
This has 3 clinical cases caused by red cell transfusion prior to 2012, and none thereafter. Given the precautionary approach adopted here, and the recommendations of the ACDP TSE Risk Assessment Subgroup, scenarios such as this are *not* included in the analysis presented in the main paper. Nevertheless, their consistency with the known data on human transmission is of some interest.

ANNEX D: SUMMARY OF "SET 2" MODEL RUNS

Prevalence inputs set to match appendix survey results: 733 (269-1596) per mn in the 1941-60 birth cohort; 412 (198 –758) infections per mn in the 1961-85 cohort.
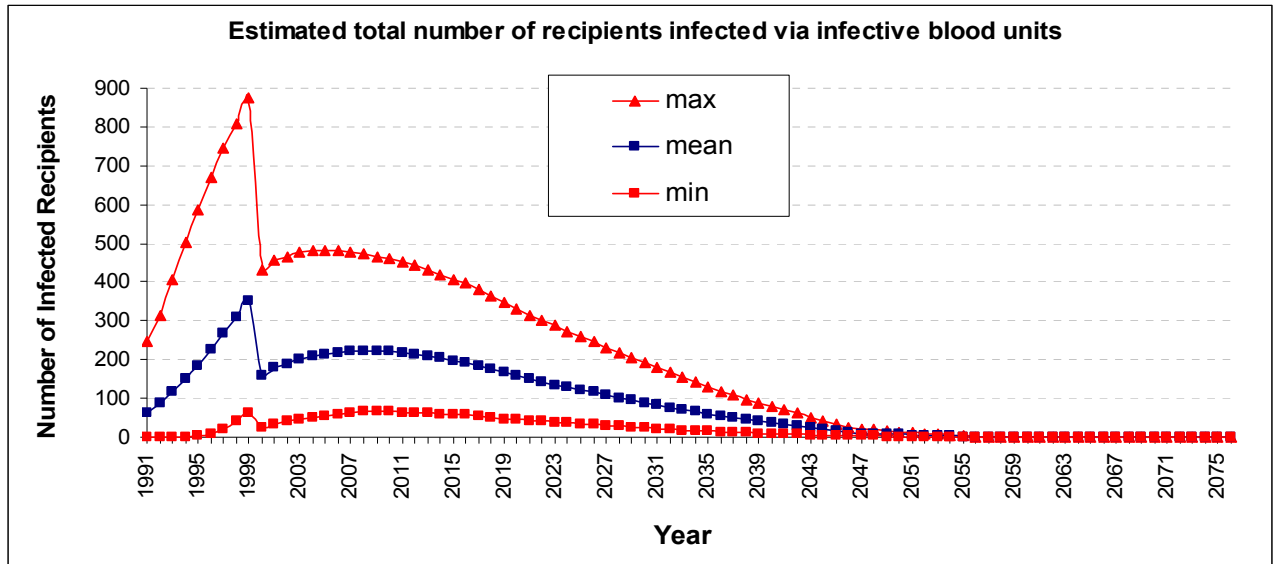
RED CELL MODEL

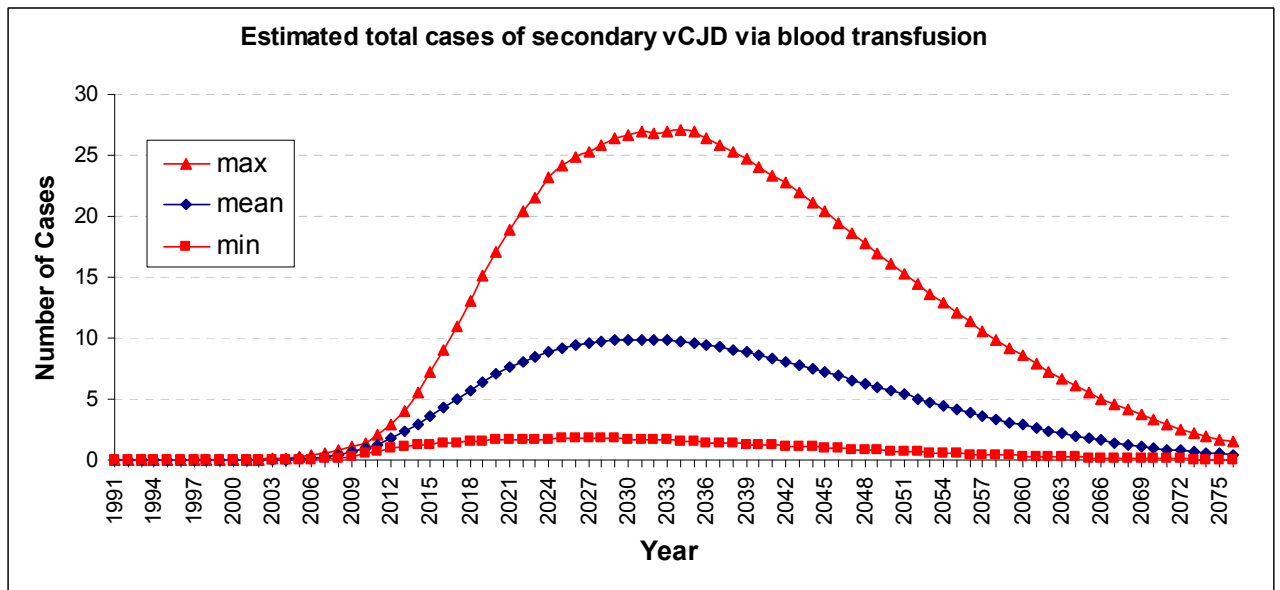**3,491 / 30,000 model runs calibrate** (3-9 clinical cases to start of 2013)

These model runs have mean IP: 24.5 years for MMs and 29 years for non-MMs, Susceptibility is 52%. The prevalence of infections in the 1941-60 and 1961-85 birth cohorts is unaffected by model calibration.

(a) No further interventions

Infections: 4020 (1070-9110) to end of 2012: 3880 (1110 - 8100) from 2013 onward

Estimated total number of recipients infected via infective blood units

Clinical Cases: 5.6 (3.1 - 8.8) to end of 2012: 350 (70-930) from 2013 onward

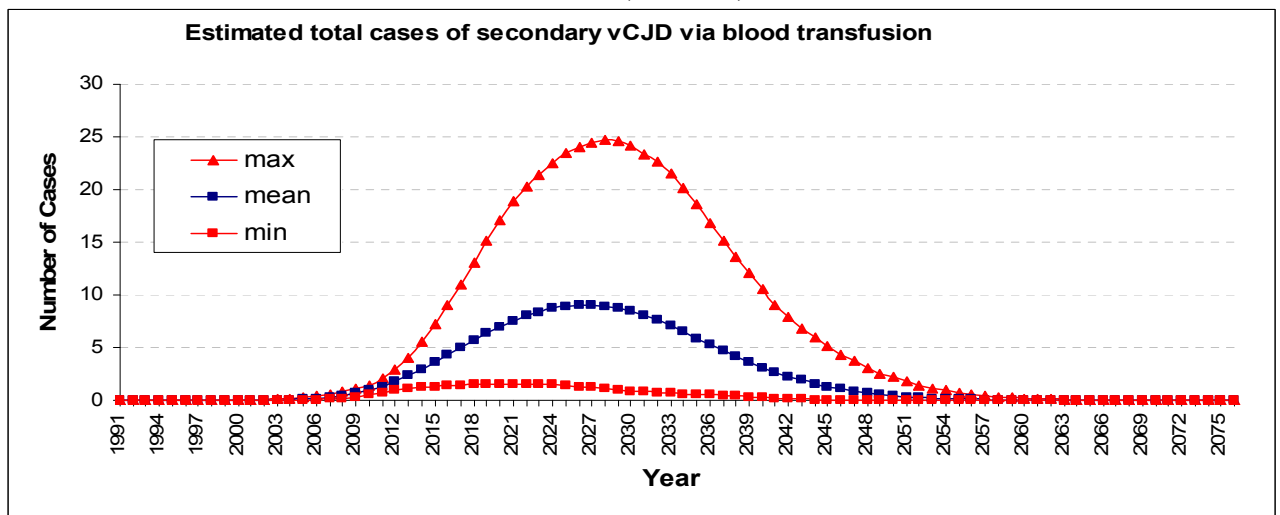Estimated total cases of secondary vCJD via blood transfusion

i
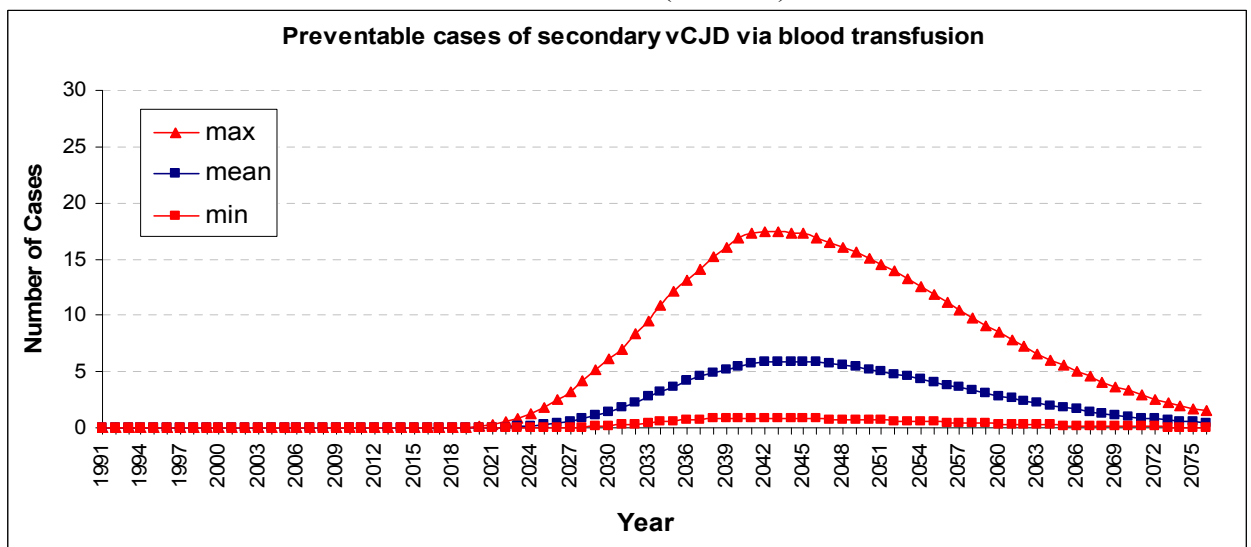
(b) With no new transmissions from end of 2012

Infections cease from 2013

Clinical Cases from 2013 onward reduce to 190 (40 - 500)

Reduction in clinical cases from 2013 onward: 160 (30 - 460)

FFP MODEL

14,587 / 30,000 model runs calibrate (0-3 clinical cases to start of 2013)

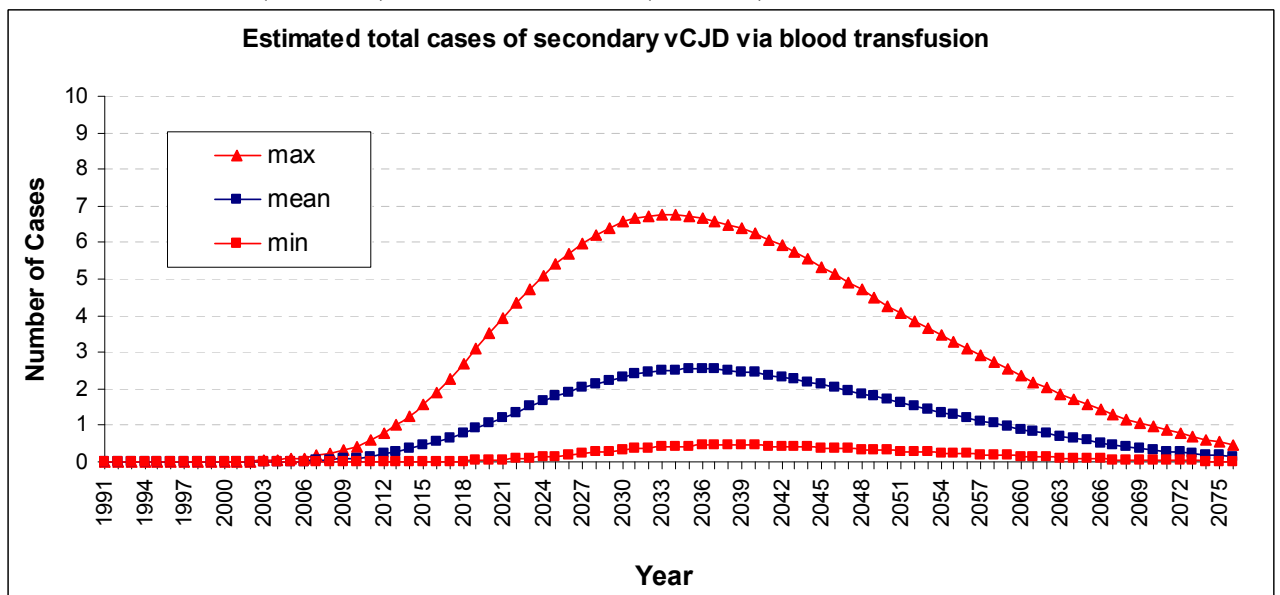These model runs have mean IP: 26 years for MMs and 30 years for non-MMs,

Susceptibility is 51%. The prevalence of infections in the 1941-60 and 1961-85 birth cohorts is similar to the starting prevalence (it decreases slightly)

(a) No further interventions

Infections: 1000 (350 – 2080) to end of 2012: 1340 (610 - 2350) from 2013 onward
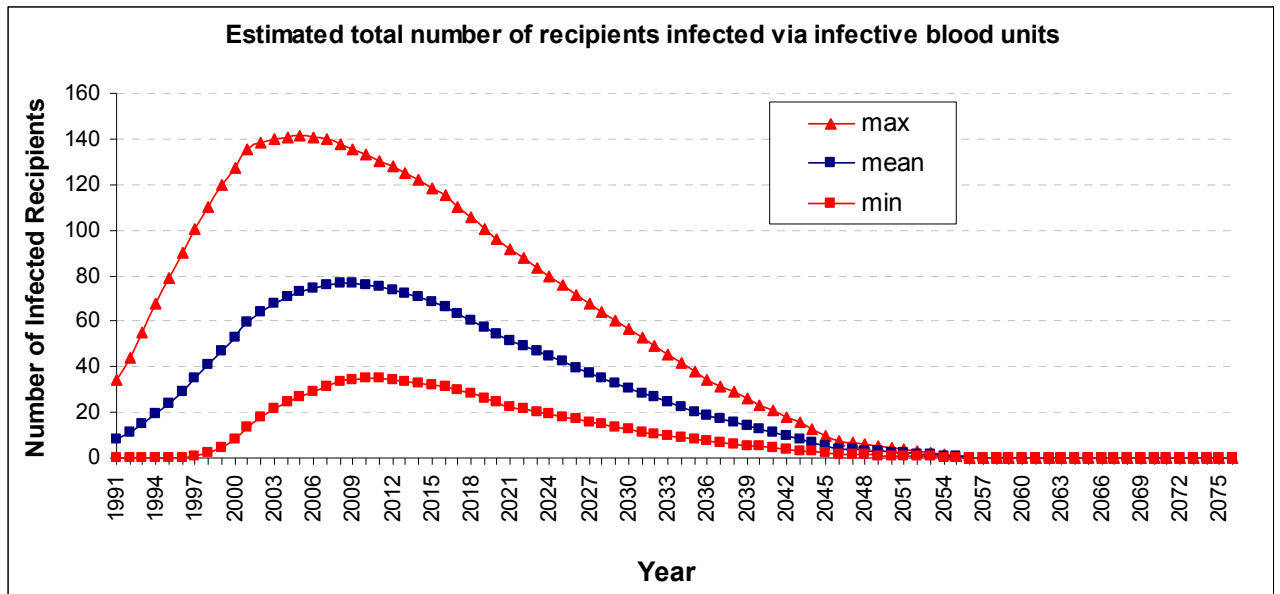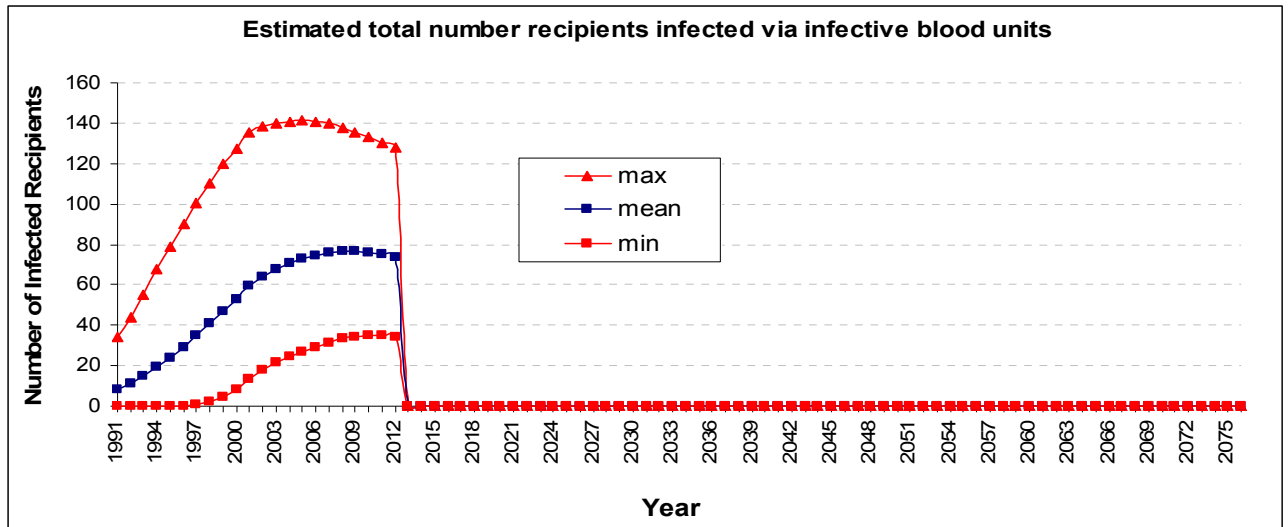

Clinical Cases: 0.7 (0.0 – 2.7) to end of 2012: 90 (20 - 220) from 2013 onward
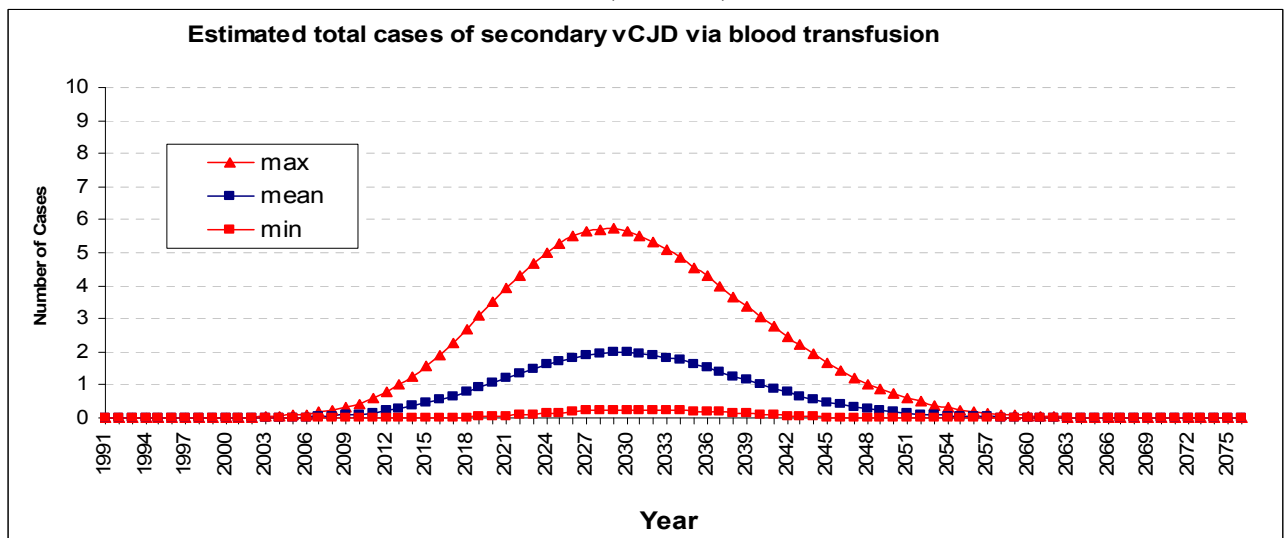
(b) No new transmissions from end of 2012

Infections cease from 2013

Estimated total number recipients infected via infective blood units

Clinical Cases from 2013 onward reduce to 40 (10 - 110)

Estimated total cases of secondary vCJD via blood transfusion

Reduction in clinical cases from 2013 onward: 50 (10 - 120)

Total preventable cases of secondary vCJD via blood transfusion

4