Low risk of variant Creutzfeldt-Jakob disease transmission from blood transfusions in Aotearoa New Zealand suggests donor exclusion policies can be relaxed

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ABSTRACT

Aotearoa New Zealand currently excludes potential blood donors who lived in the United Kingdom (UK) for 6 months or more between 1980 and 1996. This action is due to the potential for variant Creutzfeldt-Jakob disease (vCJD) following blood transfusions from pre-clinical vCJD cases, who themselves mostly developed disease from the consumption of cattle with bovine spongiform encephalopathy (BSE) during this period, or from those incubating the misfolded prion proteins that cause disease. This donor exclusion policy led to 10% of New Zealand's active blood donors in 2000 being excluded, and it remains today despite periodic shortages of some blood products. Globally there have been 232 vCJD cases recorded—178 in the UK—with no new cases since 2019 and the peak numbers 23 years ago in 2000. Only three confirmed cases have been linked to blood transfusion. Here, we aimed to estimate the annual risk of vCJD from blood transfusion in New Zealand after restriction removal. We used UK case numbers, population estimates, and donor and recipient transfusion numbers to calculate the risk to the New Zealand public. We calculated the risk, based on approximately 131,000 transfusions a year and accounting for multiple transfusions, might lead to 0.005 cases annually, or approximately one in one billion nationally, and comparable to recent one in 1.45 billion estimates for Australia. Our analyses suggests that relaxing current blood donation restrictions, like Ireland and Australia's recent policy changes, would lead to an extremely low risk of vCJD transfusion-transmission in New Zealand. This policy change would help increase the supply of blood products for multiple medical needs.

On 23 February 2023, the Aotearoa New Zealand blood service urgently needed blood. This shortage came after the service estimated in 2022 that it required 40,000 more donors in 2023 to meet demand;[1] yet, currently, New Zealand excludes potential donors who lived in the United Kingdom (UK) for 6 months or more (cumulative time) between 1980 and 1996 due to the potential for these people to be infected with variant Creutzfeldt-Jakob disease (vCJD). This exclusion led to 10% of New Zealand's active blood donors in 2000 being excluded.[2]

vCJD is a very rare but deadly degenerative brain disorder leading to dementia and death, caused by an infectious prion originally derived from eating contaminated beef and beef products.[3] It occurs against a backdrop of the far more common Sporadic Creutzfeldt-Jakob disease in humans (sCJD), which has a worldwide rate of 1–2 per million population per year and occurs spontaneously without a defined source.

The vCJD prion, PrP^{Sc}, causes bovine spongiform encephalopathy (BSE) in cattle, and this was likely derived from cattle being fed scrapie-infected sheep, another prion disease. Due to possibly long incubation periods, a lack of non-invasive tests (but see [4,5] for developments) or ways to fully remove them from products,[6] precautionary principles emphasising caution in the absence of scientific knowledge have been applied by countries to avoid any risk of vCJD from blood transfusions. However, since the first vCJD case there have only been 232 cases recorded globally, with 178 (76%) of those in the UK.[3] Further, there have been no new cases in the world since 2019, the last in UK in 2016, and the peak was in 2000, 23 years ago.[3] No new cases of transfusion-related vCJD have been reported since 2007 and there have only been three confirmed cases linked to blood transfusion ever, with a further two pre-clinical, asymptomatic cases of PrP^{Sc} detection in the spleen attributed to blood products.[3]

Due to these low numbers, countries have begun lifting restrictions on donors with potential

exposure to BSE. Ireland lifted its ban in 2019 and Australia has allowed the same demographic to donate blood from 25 July 2022.[7] Australia's exclusions were the same as New Zealand's, yet only resulted in the exclusion of 5.3% of all blood donations (50,100 donations in 1998),[8] so its impact was less than in New Zealand. The annual number of Australian blood donations made by donors potentially infected with vCJD was estimated to be 1.15 (range 0.02–31.1, based on the uncertainty in the UK prevalence estimate).[8] Indeed, recent modelling of the risk in Australia estimated the overall risk of vCJD transmission (infection) from blood, based on prior residency in and travel to the UK from 1980–1996, to be one in 389,000,000 and clinical cases one in 1,450,000,000.[9] There is no reason to believe New Zealand's will be substantially different.

If we assume the overall prevalence of vCJD among all 251,652 reported UK-born New Zealanders[10] is the same as it would be for the 176 total UK cases using the UK population in 1980 (56,310,000,[11] so, smaller than today, giving a high prevalence than larger population sizes would) then the prevalence would be 3.1×10^{-6} and we would expect fewer than one UK-born person to be a vCJD case in New Zealand (0.79). However, not all people donate blood. The New Zealand Blood Service reports 86,710 donors in 2020,[12] and initial restrictions on donors present in the UK between 1980–1996 reduced donors by 10%—so let's assume there might be 8,671 donors excluded. Using the same logic, this would mean fewer than 0.03 donors might be cases. We can assume the risk of vCJD transmission is 0.448 via blood transfusion, given 3 cases from 67 exposures.[3] Thus, 0.001 infections might take place in New Zealand per year. However, on average the 30,316 recipients received 131,308 transfusions,[12] so (accounting for multiple transfusions) infections could rise to 0.005 cases, or one in 967 million or approximately one in one billion, annually.

More rigorous, data-driven analyses, such as age-structured analyses following McManus et al.,[9] would provide more robust evidence; however, this annual risk estimate of about one in one billion is of a similarly small risk to McManus et al.'s estimates of one in 389 million for transmission and one in 1.45 billion for clinical cases for Australia that it seems unnecessary. We did not account for non-UK-born donors who might have spent 6 months or more in the UK in the prevalence estimates potentially lowering the prevalence among donors, but equally we assumed all UK born at risk, potentially increasing the prevalence among UK-born donors. By assuming all excluded donors (the 10%) from the 2020 decision were UK born potentially balances these, as some will not have been UK born. Moreover, we assumed all recipients to be at similar risk of developing vCJD, which is unlikely due to age structure at least.

A concern is there could be a second epidemic of vCJD, due to prolonged vCJD incubation periods and the number of people with sub-clinical vCJD, which is unknown.[3] In the UK one in 2,000 people are thought to carry abnormal prions; the importance of which is not known, but genetic testing for the genotype at prion protein gene (PRNP) codon 129 found most were valine homozygous in the normal population compared to methionine homozygous in vCJD cases.[13] Concerns were raised over a potential second wave from different genotypes (e.g., PRNP codon 129 MV genotype) with longer incubation periods possible after a case in the UK was detected in 2016, but such a surge has not been observed.[3] The age structure of New Zealand's blood transfusion recipients is strongly skewed, with 65% of the recipients of all New Zealand's blood component transfusions being ≥55 years old, including 20.3% aged 65–74, 19.5% aged 75–84 and 12.1% aged 85+ years in 2020.[12] Prolonged incubation periods among recipients in these age classes are less likely to be important, due to natural mortality rates from other causes and the immediate- and intermediate-term need for blood products likely being more important.

The strongest evidence of a risk from transfusion, apart from the three vCJD cases, comes from studies in sheep, where blood products have been shown to be infectious.[5] However, sCJD seems unlikely to be transmissible via blood (though iatrogenic transmission can occur via contaminated human growth hormone, dura mater and corneal grafts or neurosurgical equipment).[14,15] Moreover, there has been no second vCJD wave in the UK, which had 76% of cases, and evidence suggests extended incubation is rare in other human prion diseases, Kuru and iatrogenic CJD.[3] Modelling studies suggested a secondary blood transfusion-derived UK vCJD epidemic would be biologically implausible, with hundreds of cases considered an extreme worst case.[16] Further, the UK's own government assessment reported that future infections are expected to range from 0–62 due to 90 million transfusions spread over 50 years for red blood cells, 0–31 due to 14 million transfusions spread over the next

50 years for plasma and 0–84 due to 19 million transfusions spread over the next 60 years for platelets.[17]

In conclusion, while the risk is not zero and acknowledging the need for ongoing surveillance and that vCJD is a terrible, fatal disease, the risk of vCJD through blood transfusion in New Zealand seems extraordinarily low. Given the need for blood, and that less than 4% of the New Zealand population currently donate blood,[18] it seems time for New Zealand to revisit its own restrictions. Public health regularly requires preventative measures that carry potentially higher, but still extremely low risk. It seems timely to follow Australia and remove the restriction on donors potentially exposed to BSE in the UK in the 1980s and 1990s.

COMPETING INTERESTS
Nil.

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