Modelling the risk of transfusion transmission from travelling donors
Mapako, Tonderai; Oei, Welling; van Hulst, Marinus; Kretzschmar, Mirjam E; Janssen, Mart P

Published in:
BMC Infectious Diseases

DOI:
10.1186/s12879-016-1452-z

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2016

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Mapako, T., Oei, W., van Hulst, M., Kretzschmar, M. E., & Janssen, M. P. (2016). Modelling the risk of transfusion transmission from travelling donors. BMC Infectious Diseases, 16(143), [143]. https://doi.org/10.1186/s12879-016-1452-z

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Modelling the risk of transfusion transmission from travelling donors

Tonderai Mapako\textsuperscript{1,2,†}, Welling Oei\textsuperscript{3,4,†}, Marinus van Hulst\textsuperscript{1,5}, Mirjam E. Kretzschmar\textsuperscript{4,6,7} and Mart P. Janssen\textsuperscript{3,4}

Abstract

**Background:** The EUFRAT (European Up-Front Risk Assessment Tool) was developed as an online risk assessment tool (http://eufrattool.ecdc.europa.eu) to help decision-makers assess the transmission risk of emerging infectious diseases (EID) through blood transfusion. The aim of this study is to extend the methodology developed in the EUFRAT project to quantify the transfusion transmission (TT) risk from travelling donors.

**Methods:** A generic model for estimating the TT risk from a group of travelling donors that visited an EID risk area was developed. In addition, the new model distinguishes projected future transmissions from those that have already occurred. As an illustration the model was applied to the outbreaks of chikungunya in Italy in 2007 and Q fever in the Netherlands in 2007–2009.

**Results:** Formulas for calculating the travelling donors’ TT risk were derived. For the chikungunya outbreak in Italy an early intervention (at the end of week 7 after the start of the outbreak, so after only 19\% of all cases) would have been required to prevent only 41\% of all expected transmissions at that time. For Q fever, in which the transmission of chronic Q fever is considered, even at the end of the third annual outbreak’s peak 47\% of all (chronic) Q fever transmissions could still be prevented.

**Conclusions:** The updated model allows estimation of the infection transmission risk from travelling donors. In combination with the distinction between past and future transmissions, these estimates provide valuable information to support decisions concerning communication with the public and/or the implementation of safety interventions.

**Keywords:** Travellers’ risk, Transmission risk, Emerging infectious diseases, Blood transfusion

Background

Trends in globalisation have brought increased blood safety concerns as population members (and therefore also blood donors) have become highly mobile. This presents challenges for blood safety when travellers go to areas in which there is ongoing transmission of infectious diseases (either endemic or epidemic) and import infections to their home countries. Blood safety concerns for emerging infectious diseases (EID) are identified and documented extensively in the literature \cite{1–4}. Currently available travellers’ risk models focus mainly on the probability of travellers acquiring an infection when visiting high-risk areas \cite{5–7}, but do not link this information directly to its implications for the risk of transmission by (blood) donors.

Several blood establishments have travel risk policies for donors who report having visited EID risk areas \cite{2, 4, 6, 8–10}. Variation in existing policies may be an indication of the absence of a common understanding and perception of the blood safety risk posed by travellers in their respective home countries. The EUFRAT (European Up-Front Risk Assessment Tool) project \cite{2} developed and launched an online risk assessment tool \cite{11} to help decision-makers assess the EID risk in order to guide informed decisions concerning an appropriate course of action. The current tool, however, offers only limited opportunities for extensively analysing the transfusion transmission (TT) risk from travelling donors.

The aim of this study was to extend EUFRAT to characterise and model the risk of disease transmission from...
travelling donors to blood safety. We propose generic formulas for calculating the risk of transmission taking into account transfusions that have already occurred by the time of observation (past transmissions), and the projected (future) transmissions from travelling donors. The method was applied to the chikungunya outbreak in Italy [2, 10] and the Q fever outbreak in the Netherlands [12, 13] that have previously been analysed using EUFRAT for the TT risk among the local residents. We chose the chikungunya and Q fever examples to illustrate risk estimates for a disease with a short and a long infectious period.

Methods
Deriving the travellers risk model
For the quantification of the risk of infected donations from travellers who visited an EID risk area, a number of definitions are required. These relate to (1) the transmission in the EID risk area (number of infections notified, duration of observation, population size), (2) the infection (duration of the infectious period, proportion of symptomatic and chronic infections), and (3) the travelling donor population (number of travellers, duration of visits, donation frequency). Next, based on these definitions, formulas for the expected number of transmissions by blood transfusion from travellers were derived. A distinction is made between transmissions that have already occurred by the end of the observed outbreak (past transmissions) and for transmissions yet to occur (future transmissions).

The model of a travelling donor entering a risk area, his exposure, infection and his infectious period is illustrated in Fig. 1. A summary of parameters used in the model is given in Table 1. Details on the derivation of the formulas can be found in the Additional file 1.

We consider the situation in which a traveller enters an area with ongoing transmission of an infectious disease (which we refer to as “risk area”) at time \( t_e \), where he remains for a time period \( D_v \) after which he returns to his home country. If he becomes infected he will remain infectious for a period \( D_i \) and in case he donates within this time period upon returning home, he is expected to transmit the infection acquired. Thus, the exposure of the traveller begins upon entering the risk area at \( t_e \) and lasts for a period \( D_v \). Because we are interested in the donations made by the traveller after the end of his visit \( D_v \), the time being infectious while able to donate is defined as the time interval from \( t_e + D_v \) to \( t_i + D_i \). Let us call this interval \( D_x(t_e + D_v) \), which is relevant for transfusion transmission. All time intervals are presumed to be non-negative.

We assume that transmission in the area during the risk assessment can be characterised by a constant incidence rate \( \lambda = \frac{I}{ND_o} \), where \( I \) is the number of infections notified in the time interval \( D_o \) corrected for underreporting, \( N \) is the size of the population at risk, and \( D_o \) is
Table 1 Description of model parameters and their values used in estimating travellers transmission risks for the respective chikungunya [2, 10] and Q fever [1, 3] outbreaks

| Symbol | Dimension | Description | Chikungunya | Q fever |
|--------|-----------|-------------|-------------|---------|
| \( \lambda \) | - | Incidence rate: the rate of infection accrual in the risk area. | \( 5.9 \times 10^{-7} \) per day | \( 1.4 \times 10^{-5} \) per day |
| \( N \) | - | Population size: the size of the local population in the risk area. | 3,977,508 | 55,725 |
| \( D_{to} \) | Time | Duration of the observation: the time from the 1st day of reported cases until the day of the last reported case; or for a series of observations: the time from the start until the end of each observation period. | 105 days (15 weeks) | 1050 days (35 months) |
| \( p_d \) | - | Proportion of donors: the proportion of donors among the general population. | 3.53% \(^a\) | 2.37% \(^a\) |
| \( \tau = p_d f_v \) | - | Rate of donors visiting the risk area: this is calculated from a proportion of donors \( p_d \) among the number of visitors to the risk area per unit time \( (f_v) \). | 0.35 donors/day \(^a\) | 0.24 donors/day \(^a\) |
| \( \varphi = \frac{1}{t} \) | 1/time | Donation rate: number of donations per unit time, this depends on the inter-donation interval \( (D_i) \), i.e. time in between subsequent donations by donors. | 0.005 per day \(^a\) (\( D_i = 215 \)) | 0.005 per day \(^a\) (\( D_i = 215 \)) |
| \( D_v \) | Time | Duration of infectious donation period: the time in which a traveller might give blood transfusion during his infectious period after returning home. | 7 days \(^a\) | 14 days \(^a\) |
| \( t \) | Time | Time the time since the start of the observation. | | |
| \( t_e \) | Time | Time of donor entry: the time at which a travelling donor arrives in the risk area within the observation period. | | |
| \( t_i \) | Time | Time of infectivity: the time at which the travelling donor is presumed to obtain an infection. | | |
| \( t_f \) | Time | Time of donation: time at which an individual donor is assumed to deliver an infected donation. | | |
| \( N_c \) | - | Number of transmissions - from travelling donors after returning to their home country. | | |
| \( N_{cf} \) | - | Number of future transmissions – from travelling donors after the end of the so far observed transmission; so after time point \( t_{obs} \). | | |

\(^a\)Fictive parameter values or assumptions

The number of transmissions per infected donor would generally be proportional to the donation rate \( (\varphi) \) and the duration of the infectious period \( (D_i) \). For travelling donors however, half the duration of the visiting time is subtracted from the infectious period. This makes sense as donors will not be able to donate during their visit to the risk area and therefore the infectious period of a visiting donor will on average be reduced by half the visiting time.

\[ N_v = \int_{t_f=0}^{D_v} \int_{t_e}^{t_f+D_i} \int_{t_i=0}^{\min(D_h, t_e)} t \lambda \varphi dt_e dt_i dt_f \]

\[ = \frac{1}{2} D_v \tau \lambda \varphi (2D_f - D_v) D_v = \frac{D_v T}{N} \lambda \varphi \left( \frac{1}{2} D_v \right) \]

(1)
For those cases where $t_e + D_v < t_{obs}$, a fraction of the total number of infected donations are expected to have already been made at the time of observation $t_{obs}$. Such transmissions cannot be prevented any more. The remaining fraction, however, can potentially be prevented by an intervention in the blood supply. This remaining fraction can be determined by splitting the formula into transmissions occurring before $t_{obs}$ (past), and transmissions after $t_{obs}$ ($=D_o$) (future):

$$N_v = \int_{t_e = -D_o}^{D_o} \int_{t_e + t_i = \text{max}(t_e, 0)}^{t_i = \text{max}(t_e, 0)} \tau \lambda \phi(t_i + D_i - D_v) dt_i dt_e + \int_{t_e = -D_o}^{D_o} \int_{t_i = t_e + t_i}^{t_e} \tau \lambda \phi(t_i + D_i - D_v) dt_i dt_e$$

Thus, the number of future transmissions from traveling donors ($N_{cf}$) expected at $t_{obs}$ for $t_e + D_v < t_{obs}$ can be calculated as:

$$N_{cf} = \int_{t_e = -D_o}^{D_o} \int_{t_e + t_i = \text{max}(t_e, 0)}^{t_i = \text{max}(t_e, 0)} \tau \lambda \phi(t_i + D_i - D_v) dt_i dt_e$$

(2)

For situations in which the infectious period is longer than the duration of stay ($D_v > D_o$), the number of future transmissions (so transmissions that will occur after $t_{obs}$) is equal to:

$$N_{cf} = \begin{cases} 
\frac{\tau \lambda \phi(3D_v^2 - D_o^2)}{6ND_0} & \text{if } D_v \geq D_0 \geq D_v \\
\frac{\tau \lambda \phi(6D_vD_o - 3D_v^2 - D_o^2)}{6ND_0} & \text{if } D_v \geq D_0 \geq D_v \\
\frac{\tau \lambda \phi(6D_vD_o - 3D_v^2 - D_o^2)}{6N} & \text{if } D_v \geq D_0 \geq D_v 
\end{cases}$$

(3)

As donors can potentially transmit infection long after becoming infected (e.g. in the case of chronic infections) the distinction between past and future transmissions can be informative. This allows a decision maker to assess the impact of safety interventions and the necessity for communication of risks to transfusion recipients even at the end or (long) after an outbreak has occurred.

In situations where $D_i < D_v$ and the infection occurs at the beginning of the visit, so within $D_v < D_i$ after entering the risk area, the infectious period has already passed before the donor returns home and no transmission will occur. This means that the duration of exposure with a risk of transmission had length $D_i$ instead of $D_v$ and the risk of transmission has to be corrected for the likelihood of an early infection. The risk of the donor getting infected in this first period of his visit is equal to $\lambda(D_v - D_i)$. Hence the number of (future) infected donors can be calculated using Eqs. 1 and 3 whilst replacing the duration of the visit by the length of the infectious period ($D_i$) and noting that the risk is overestimated by a (most likely very small) factor $1/(1 - \lambda(D_v - D_i))$.

The estimated number of infected donations might have to be adjusted according to the proportion of under-reporting of notified cases, according to the time that infected donors will actually donate during their infectious period before symptom onset (referred to as the critical infectious period in the original EUFRAT model), or adapted for the infectivity of the specific transfused product [2]. In addition, if more than one (infectious) product is derived from one donation, the number of transmissions will have to be adjusted accordingly.

### Application to outbreak data and sensitivity analysis

The travellers’ risk model was applied to the chikungunya outbreak in Italy in 2007 [2, 10]. We illustrate the risk for a group of non-Italian travellers, for instance from country A, who went to Italy during the outbreak and donate upon return in their home country. The analysis was done using the reported weekly number of infections in the outbreak region, corrected for the proportion of asymptomatic infection. To address the variation in incidence rates over time, the outbreak is modelled as a series of independent weekly outbreaks; thus the formulas were applied sequentially and the resulting estimated transmissions aggregated. To illustrate the sensitivity of the risk estimates to variation in model parameters, the numbers of transmission transmissions were calculated for various values for the duration of stay and for the infectious period.

As a second example the Q fever outbreak, which lasted for over a 3-year period in the Netherlands, was assessed for the transmission risk of chronic Q fever in non-Dutch travellers to the Netherlands [12]. The monthly number of notified Q fever cases used in the analysis can be found in Additional file 1: Table S3. Note that the infectivity of chronic Q fever, in terms of pathogenicity and length of the infectious period, differs from that of the acute infection. Also, chronically infected travellers may be less likely to donate due to their underlying disease/condition (such as a heart valve abnormalities) [14, 15]. Nevertheless, we used chronic Q fever transmission to illustrate the risk from an infection with a long infectivity period. It is presumed that 2% of the infections progress to a chronic infection with an infectious period of 12 months.

### Computer software

All formulas were derived using Mathematica (version 9.0.1, The Wolfram Centre Lower Road, Long Hanborough, Oxfordshire, United Kingdom). The formulas were implemented in Microsoft Excel (MS Office Professional Plus 2010, Excel version 14.0, Microsoft Corporation, One Microsoft Way Redmond, WA 98052–7329 USA) for analysis and graphing.
Results

Application to the chikungunya outbreak in Italy

Weekly chikungunya infections reported during the 15-week outbreak in Italy in 2007 were used to estimate the total number of transmissions by blood transfusion from travellers to Italy, as well as the expected proportion of future transmissions. The number of chikungunya infections was estimated by adjusting the notified cases for the proportion of asymptomatic cases (15%); we used the adjusted value to allow for a comparison with earlier results. The expected future transmissions are shown in Table 2 and Fig. 2 for a scenario in which ten travellers per day (\( r = 10 \)) visited the risk area, remaining in the area for 7 days each (\( D_v = 7 \)). For this scenario, the total cumulative (15 weeks) travellers’ transmission risk is 4.45 per million blood donations from travellers to Italy. At the end of outbreak week 7, the total number of expected transmissions is 0.85 per million and the proportion of future transmissions – given that 19% of all infections were observed by the end of week 7 – is 41%. Implementation of interventions like stopping blood collection at this early stage only would substantially mitigate future transmissions from donors that travelled to the risk area.

Sensitivity analysis

First, the duration of visit was varied. For duration of the travellers’ visit of 2, 4, and 8 days, the total transmission risk is equal to 2, 3.4 and 4.5 per million, respectively. Given that the infectious period is 8 days, the duration of the visit from 8 days onwards will result in a similar transmission risk for this setting. What can be observed is the decreasing relative increase in the number of transmissions with increasing visit length as a result of the negative quadratic term in visit length in Eq. 1. Here one can see that a four-fold increase in the duration of visit only doubles the risk. Therefore only for (relatively) short visits will the risk be linear in the duration of visit.

Next, the duration of visit was assessed for an infectious period of 1 year (365 days). Now the observed transmission risk becomes 100, 200, 410 and 710 per million for respective visit lengths of 2, 4, 8 and 14 days. Here it can be noted that the risk from travelling donors increases almost linear with the duration of visit (14/2 \( \times \) 100 \( = \) 700 \( \approx \) 710). The proportion of future transmissions at any given time during and after the outbreak period will be closely similar for each of these scenarios, as most transmissions (approximately 87%) will occur after the end of the observed outbreak.

Application to the Q fever outbreak in the Netherlands

Using the disease parameters from a previous Q fever study and visit characteristics as provided in Table 1 for analyses of the chikungunya outbreak, the number of...
transmissions from donors visiting the risk area in the Netherlands can be calculated. A constant stream of 10 visitors per day who on average stay for 2 weeks in the risk area would result in a total of 1.7 per thousand infection transmissions in the home country. Note that this number is derived directly from the number of notified cases (presuming 2 % chronic cases), whereas in the Q fever study the estimate was influenced by a proportion of more than 90 % undetected cases and a 50 % probability that symptomatic donors were screened out by the donor health questionnaire. The monthly outbreak analyses from the high-risk area indicated that at the annual outbreak peaks in 2007 (month 3, 36 cases), 2008 (month 15, 121 cases) and 2009 (month 27, 159 cases), the percentage of future transmissions are 95, 70 and 47 %, respectively, as shown in Fig. 3.

It is clear that incorporating uncertainty in all model parameters would allow construction of credible intervals (CIs) around the estimated number of transmissions. However, the figures are provided for illustration of the application of the methodology rather than for estimating the number of transmissions, hence CIs are not provided.

**Discussion**

Our study shows that it is feasible to estimate the number of transmissions from travelling donors by applying the travellers’ risk model described in this paper. The model developed can support decision-making concerning safety interventions and communication related to donors travelling to EID risk areas. The model allows –using only a few basic parameters related to the outbreak, the infectious disease, and the travelling donor population– estimation of the transmission risk from travelling donors.

For the chikungunya outbreak we noted that the estimated traveller’s risk for a 1 week visit is 0.1 per million (0.1 infections in 1,000,000 donations made by travellers to the outbreak region). Liumberno and colleagues reported that during this outbreak a 21-day deferral policy was implemented nationally for all donors who had visited the risk area even for a few hours, although their acceptable cut-off risk is one in 380,000, which is much higher than our model’s estimate [10]. Had the travellers’
risk model been available at that time, the policy might have been different. Chikungunya has only a short infectious period of 8 days. Therefore, only a limited number of future infections are anticipated. The ability of the travellers risk model to generate the expected number of future infections allows decision makers to quantify the potential immediate impact of (in)action on transfusion safety.

One of the limitations of our model is that it assumes that travelling donors only visit the risk area once. In some cases, travellers might make recurring visits and such repeated exposures might further increase their susceptibility to infection. This was also noted by Massad and colleagues [5]. For asymptomatic dengue infections repeat travel could expose a previously infected traveller to more severe expressions of illness, which might affect the donation behaviour of travellers. Data on such travel behaviour may not be easily available however. Another limitation of our model is that it presumes fixed donation intensity whereas donation behaviour is likely not to be constant in time, especially around periods of travel. When such information is available however, there are no restrictions to include these in modelling the risk of infected donations. Also, the current model presumes that the infection is transmissible immediately after infection. However, in case a disease is only infectious after a particular incubation time $D_i$, the risk from such an infection can be calculated by simply calculating the number of infections that would have been transmitted if infections would have been transmitted over the full infectious period $D_i$ and subtracting the infections transmitted from the time of infection up until the incubation time $D_i$.

We noted that the travellers’ risk model is generally applicable, and its application is illustrated for two real outbreaks. Our model, with its distinction between past and future transmissions, can be considered a useful extension to currently available models for estimating transfusion transmission risks. Application of the travellers’ risk model may assist blood establishments in harmonising risks posed by travelling donors [9]. Several studies have shown that travellers do pose a risk [8, 16] which requires blood authorities to have mechanisms in place to manage such risks.

The example applications in this paper assumed 100 % transmissibility of the infection during the infectious period that will provide conservative risk estimates. The web based EUFRAT model however allows specification of the probability of transmission per type of transfusion product (which are typically red cells, platelets or plasma). It should be noted that transfusion transmission for chikungunya has not yet been demonstrated [10], and for Q fever the single suspected transmission case reported was not conclusively confirmed [12, 17]. Nevertheless, despite the unavailability of evidence concerning the transmission rate, decision-makers would still be interested in the expected number of transmissions for various viable scenarios. Such scenario analyses can only be conducted if models for calculating the transmission risks are available.

Conclusions

We have developed a model that allows estimation of transfusion transmission risk from travelling donors. The limited number of generic model parameters required permits the model to be applied in very diverse settings. This not only empowers public health decision-makers with an appropriate tool to objectively quantify the risk from traveling donors, but also provides a sound proactive basis for enhanced management and response to outbreak situations.

Additional file

Additional file 1: Deriving the risk of transfusion transmission from travelling donors. (DOCX 91 kb)

Abbreviations

BD: emerging infectious diseases; TT: transfusion transmission.

Competing interests

The authors declare that they have no competing interest.

Authors’ contribution

TM initiated the study, carried out data analysis, and wrote an early version of the manuscript. WO continued with generating and checking formulas, data analysis, and wrote the final manuscript. RvH participated in the study design, coordination and helped to draft the manuscript. MEX checked the formulas derived and improved the manuscript. MPJ was responsible for the conception of the research, coordinated the study, and improved the manuscript. All authors have read and agreed with the final version of the manuscript.

Acknowledgements

We would like to thank Roel Coutinho and Hans Zaaljer for their critical insights while writing this paper.

This study was supported by Sanquin Blood Supply Foundation and the T-REC project funded by the European Union Seventh Framework Programme (FP7/2007–2013) under grant agreement n° 266194.

Author details

1. Unit of PharmacoEpidemiology & PharmacoEconomics (PE2), Department of Pharmacy, University of Groningen, Groningen, The Netherlands. 2. National Blood Service Zimbabwe, Harare, Zimbabwe. 3. Transfusion Technology Assessment Unit, Sanquin Research, Amsterdam, The Netherlands. 4. Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands. 5. National Institute for Public Health and the Environment, Bilthoven, The Netherlands. 6. National Institute for Public Health and the Environment, Bilthoven, The Netherlands. 7. National Institute for Public Health and the Environment, Bilthoven, The Netherlands. 8. National Institute for Public Health and the Environment, Bilthoven, The Netherlands. 9. National Institute for Public Health and the Environment, Bilthoven, The Netherlands. 10. Center for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands.

Received: 27 May 2015 Accepted: 3 March 2016

Published online: 01 April 2016

References

1. Allain JP. Emerging viruses in blood transfusion. Vox Sang. 1998;74:125–9.
2. Oei W, Janssen MP, van der Poel CL, van Steenbergen JE, Rehmet S, Kretzschmar MEE. Modeling the transmission risk of emerging infectious diseases through blood transfusion. Transfusion. 2013;53:1421–8.
3. Stramer SL, Holliger FB, Katz LM, Kleinman S, Metzel PS, Gregory KR, Dodd RY. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion. 2009;49 Suppl 2:S1–S29.

4. Wilder-Smith A, Chen LH, Massad E, Wilson ME. Threat of dengue to blood safety in dengue-endemic countries. Emerg Infect Dis. 2009;15:8–11.

5. Massad E, Rocklov J, Wilder-Smith A. Dengue infections in non-immune travellers to Thailand. Epidemiol Infect. 2013;141:412–7.

6. O’Brien SF, Utzicanin S, Choquet K, Yi QL, Fan W, Goldman M. Impact of changes to policy for Mexican risk travel on Canadian blood donor deferrals. Blood Transfus. 2013;11:80–4.

7. Massad E, Behrens RH, Burattini MN, Coutinho FA. Modeling the risk of malaria for travelers to areas with stable malaria transmission. Malar J. 2009;8:296.

8. Grande R, Petritri G, Silvani I, Simoneschit B, Marconi M, Torresani E. Immunological testing for malaria and blood donor deferral: the experience of the Ca’ Granda Polyclinic Hospital in Milan. Blood Transfus. 2011;9:162–6.

9. Leiby DA, Nguyen ML, Notari EP. Impact of donor deferrals for malaria on blood availability in the United States. Transfusion. 2008;48:2222–8.

10. Liumbruno GM, Caleri D, Petrupulacos K, Mattivi A, Po C, Macini P, Tomasinj I, Zucchelli P, Silvestri AB, Sambri V, Pupella S, Catalano L, Piccinini V, Calizani G, Grazzini G. The Chikungunya epidemic in Italy and its repercussion on the blood system. Blood Transfus. 2008;6:199–210.

11. The European Up Front Risk Assessment Tool. http://eufrattool.ecdc.europa.eu. Accessed on 24 January 2016.

12. Oei W, Kretzschmar MEE, Zaaijer HL, Coutinho R, van der Poel CL, Janssen MP. Estimating the transfusion transmission risk of Q fever. Transfusion. 2014;7:1705–11.

13. Van der Hoek W, Dijkstra F, Schimmer B, Schneeberger PM, Vellemeen P, Wijkman C, ter Schegget R, Hackert V, van Duynhoven Y. Q fever in the Netherlands: an update on the epidemiology and control measures. Euro Surveill. 2010;15:12.

14. Kampschreur LM, Dekker S, Hagemans JC, Leestrae PJ, Renders NH, de Jager-Leclercq MG, Hermans MH, Groot CA, Groenwold RH, Hoepelman HI, Wever PC, Oosterheert JJ. Identification of risk factors for chronic Q fever, the Netherlands. Emerg Inf Dis. 2012;18:563–70.

15. Slot E, Hogema BM, Moller M, Zaaijer HL. Screening of blood donors for chronic Coxiella burnetti infection after large Q fever outbreaks. Transfusion. 2014;54(11):2867–70.

16. Cobelens FG, Groen J, Oosterhaus AD, Leentvaar-Kuipers A, Wertheim-van Dillen PM, Kager PA. Incidence and risk factors of probable dengue virus infection among Dutch travellers to Asia. Trop Med Int Health TM IH. 2002;7:331–8.

17. Van Kraaij MG, Slot E, Hogema BM, Zaaijer HL. Lookback procedures after postdonation notifications during a Q fever outbreak in the Netherlands. Transfus Clin Biol. 2013;53:716–21.