Online estimation of the risk of blood contamination

Welling Oei

Transfusion Technology Assessment (TTA) Group
Julius Center for Health Sciences and Primary Care, UMC Utrecht, The Netherlands

IPFA/PEI 19th International Workshop on Surveillance and Screening of Blood Borne Pathogens
23 May 2012
MITCH and EUFRAT projects

Modelling emerging Infections in the Transfusion CHain (MITCH)
– to provide a decision support model that quantifies decision elements that play a role in the decision making with respect to blood safety measures to be taken in case of outbreaks of EIDs.

European Up-Front Risk Assessment Tool (EUFRAT)
– to develop a web-based calculator for estimating the crude risk of receiving contaminated blood donations for a range of communicable diseases in outbreak situations.
Methods

- Literature review of emerging infectious diseases (EIDs) in transfusion medicine ✓
- Development of a risk prioritization algorithm (70 diseases) ✓

Development of a generic model to quantify the risks of transfusion transmission of EIDs ✓

- Organized an expert meeting to test the model and select most relevant EIDs to include in the model ✓

Convert the model into a web-based tool (EUFRAT) ✓

Test/validate the model with EID examples
EUFRACT --STEP 1-- Estimating the prevalence of infection in the donor population

\[ P = \frac{I_p R_d \min(t_a, d) + \kappa \min(t_c, d)}{N_p d (1 - \nu)} \]
EUFRAT -- STEP 2 --
Estimating number of infected donations

Donor health questionnaire
Compliance ($Q_c$) & effectiveness ($Q_e$)

<table>
<thead>
<tr>
<th>Donors</th>
<th>Recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>Healthy</td>
</tr>
<tr>
<td>Symptomatically infected ($I_s$)</td>
<td>Healthy</td>
</tr>
<tr>
<td>Symptoms manifest later</td>
<td>Infected</td>
</tr>
<tr>
<td>Asymptomatically infected</td>
<td>Infected</td>
</tr>
</tbody>
</table>

Symptomatically infected ($I_s$)

Infectivity level

- Acute
- Chronic

Symptom onset

($T_{ais}$) ($T_{ais}$) ($T_{cis}$) ($T_{cia}$)

Critical infectivity
EUFRAT -- STEP 3 -- Estimating number of infected components

Input: existence of screening test
- Coverage ($T_c$)
- Effectiveness ($T_e$)
EUFRAT -- STEP 4 --
Estimating number of infected end products

Interventions:
1. Pathogen inactivation or removal
2. Blood processing: leukofiltration, washing, freezing, thawing, storage, others

Preparation units ($u$)
- Donations
  - Whole blood
- Blood products
  - Red blood cells
  - Platelets
  - Plasma products
EUFRAT -- STEP 5 --
Estimating number of infected recipients

Input:
• Specific immunity in recipients ($R_i$)
• Disease severity distribution ($S$, $CR$, $M$)
Test the model with chikungunya outbreak example

Parameters input:

- 247 cases reported from an area with population of 3,977,508 during fifteen weeks of outbreak.
- 85% infected develop symptoms, infectious period of 2 and 8 days for sympt. and asympt infection.
- Donors 2% of total population donate WB twice a year
- Assumptions: donated blood is fully infectious for recipients.

Liumbruno et al. The chikungunya epidemic in Italy. Transfusion. 2008. 6(4):199-210
Quantify the risk of transfusion transmission in an outbreak-affected region OR from a donor who has visited that region.

Please indicate if you have information listed below:

1. Do you want to estimate the risk of transfusion transmission from a donor who has visited an outbreak-affected region? (no)
2. Is the number of infected donors known? (no)
3. Is information on various donation types and frequencies available? (no)
4. Are there questions in the donor health questionnaire that potentially screen out the infected donors before donation? (yes)
5. Is the donated blood screened for the infection using a diagnostic test? (no)
6. Is pathogen removal/inactivation or blood processing implemented to minimize the risk of contamination? (no)

(Donor) population infectivity

<table>
<thead>
<tr>
<th>Population exposure &amp; susceptibility</th>
<th>Value</th>
<th>Unit</th>
<th>Type</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population size (N)</td>
<td>3977508</td>
<td>[-]</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Cumulative infections reported (Ip)</td>
<td>175</td>
<td>[-]</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Duration of epidemic (D)</td>
<td>70</td>
<td>days</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Duration of infectivity for acute (Ta) infection</td>
<td>8</td>
<td>days</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Proportion of chronic infection (%C)</td>
<td>0</td>
<td>%</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Duration of infectivity for chronic infection (Tc)</td>
<td>0</td>
<td>days</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Proportion of undetected cases (%U)</td>
<td>15</td>
<td>%</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor exposure &amp; susceptibility</th>
<th>Value</th>
<th>Unit</th>
<th>Type</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor relative risk (RR)</td>
<td>100</td>
<td>%</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
<tr>
<td>Prevalence of infection in the donor population (Pd)</td>
<td>0.59</td>
<td>per 100,000</td>
<td>Const</td>
<td>✓ Valid value</td>
</tr>
</tbody>
</table>
### Donation Infectivity

#### Donation Types

<table>
<thead>
<tr>
<th>Donation types</th>
<th>Minimum</th>
<th>Mode</th>
<th>Mean (outputs)</th>
<th>Maximum</th>
<th>Unit</th>
<th>Type</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor population size (d)</td>
<td>140216</td>
<td>140216</td>
<td>[-]</td>
<td>Const</td>
<td>✓</td>
<td>Valid value</td>
<td></td>
</tr>
<tr>
<td>Expected number of infected donations before donor health questions (pID)</td>
<td>0.04</td>
<td>0.04</td>
<td>[-]</td>
<td>Const</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compliance with donor health questionnaire (Qc)</td>
<td>97.60</td>
<td>97.60</td>
<td>%</td>
<td>Const</td>
<td>✓</td>
<td>Valid value</td>
<td></td>
</tr>
<tr>
<td>Effectiveness of donor health questionnaire (Qe)</td>
<td>99.999</td>
<td>99.999</td>
<td>%</td>
<td>Const</td>
<td>✓</td>
<td>Valid value</td>
<td></td>
</tr>
<tr>
<td>Proportion of symptomatic infection (%s)</td>
<td>85</td>
<td>85</td>
<td>%</td>
<td>Const</td>
<td>✓</td>
<td>Valid value</td>
<td></td>
</tr>
<tr>
<td>Critical infectivity amongst symptomatic acute infection (Tais) Range: [0, 8]</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>days</td>
<td>Rand</td>
<td>✓</td>
</tr>
<tr>
<td>Critical infectivity amongst symptomatic chronic infection (Tcis) Range: [0, 0]</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>days</td>
<td>Const</td>
<td>✓</td>
<td>Valid value</td>
</tr>
<tr>
<td>Critical infectivity amongst asymptomatic acute infection (Taia) Range: [0, 8]</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>days</td>
<td>Rand</td>
<td>✓</td>
</tr>
<tr>
<td>Critical infectivity amongst asymptomatic chronic infection (Tcia) Range: [0, 0]</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>days</td>
<td>Const</td>
<td>✓</td>
<td>Valid value</td>
</tr>
<tr>
<td>Number of infected donations (ID)</td>
<td>4.30e-3</td>
<td>0.01</td>
<td>0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### (Donor) population infectivity

<table>
<thead>
<tr>
<th>Donor exposure &amp; susceptibility</th>
<th>Minimum</th>
<th>Mode (inputs) Mean (outputs)</th>
<th>Maximum</th>
<th>Unit</th>
<th>Type</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of infection in the donor population (PD)</td>
<td></td>
<td>0.62</td>
<td></td>
<td>per 100,000</td>
<td>Const</td>
<td></td>
</tr>
</tbody>
</table>

### Donation infectivity

<table>
<thead>
<tr>
<th>Risk of infected donations</th>
<th>Minimum</th>
<th>Mode (inputs) Mean (outputs)</th>
<th>Maximum</th>
<th>Unit</th>
<th>Type</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected number of infected donations before donor health questions (PID)</td>
<td></td>
<td>0.04</td>
<td></td>
<td>[-]</td>
<td>Const</td>
<td></td>
</tr>
<tr>
<td>Number of infected donations (ID)</td>
<td>4.36e-3</td>
<td>0.01</td>
<td>0.03</td>
<td>[-]</td>
<td>Rand</td>
<td></td>
</tr>
</tbody>
</table>

### Released component infectivity

<table>
<thead>
<tr>
<th>Risk of infected released components</th>
<th>Minimum</th>
<th>Mode (inputs) Mean (outputs)</th>
<th>Maximum</th>
<th>Unit</th>
<th>Type</th>
<th>Validation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of infected released components (IRL)</td>
<td>4.36e-3</td>
<td>0.01</td>
<td>0.03</td>
<td>[-]</td>
<td>Rand</td>
<td></td>
</tr>
</tbody>
</table>

### End product infectivity

<table>
<thead>
<tr>
<th>Risk reduction interventions</th>
<th>RBC</th>
<th>Platelets</th>
<th>Plasma</th>
<th>Plasma derived products</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of infected end products (IIP)</td>
<td>0.01</td>
<td>0.01</td>
<td>0.14</td>
<td>0.03</td>
<td>[-]</td>
</tr>
</tbody>
</table>

### Risk of infection in recipient

<table>
<thead>
<tr>
<th>Recipient reaction</th>
<th>Total</th>
<th>RBC</th>
<th>Platelets</th>
<th>Plasma</th>
<th>Plasma derived products</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of severe infection (pRs)</td>
<td>2.03e-4</td>
<td>1.45e-5</td>
<td>1.45e-5</td>
<td>1.45e-4</td>
<td>2.90e-5</td>
<td>[-]</td>
</tr>
<tr>
<td>Risk of chronic infection (pRc)</td>
<td>0.00e+0</td>
<td>0.00e+0</td>
<td>0.00e+0</td>
<td>0.00e+0</td>
<td>0.00e+0</td>
<td>[-]</td>
</tr>
<tr>
<td>Risk of death from infection (pRd)</td>
<td>2.03e-4</td>
<td>1.45e-5</td>
<td>1.45e-5</td>
<td>1.45e-4</td>
<td>2.90e-5</td>
<td>[-]</td>
</tr>
<tr>
<td>Risk of infection due to infected end product (pRTt)</td>
<td>0.20</td>
<td>0.01</td>
<td>0.01</td>
<td>0.14</td>
<td>0.03</td>
<td>[-]</td>
</tr>
</tbody>
</table>
EUFRAT: chikungunya outbreak example

Alternative scenario:

• A donor donates 1 day after visiting the area for one week → probability of being infectious is 0.49 (95%CI, 0.01-0.65) per 100,000.

• If DHQ exists with compliance of 97.6% and effectiveness of 35%, he is at risk of giving infected donations of 0.26 (95%CI, 0.09-0.5) per 100,000.
EUFRAT: chikungunya outbreak example

Liumbruno et al. The chikungunya epidemic in Italy. Transfusion. 2008. 6(4):199-210
Model validation using Q fever outbreak in NL

1. Notifications data:
   Q fever confirmed cases of 373 from high risk areas (1 June 2009 to 31 January 2010) with a population of 86,245.

2. An independent donation screening study reveals three out of 1004 serum samples collected from 762 donors tested positive for C. burnetii DNA and by IFA for presence of IgG phase II (prevalence of 393.70 per 100,000).

EUFRAT estimates the prevalence of infection to be 484.93 (95%CI, 296.35-794.30) per 100,000.

Q fever outbreak in NL

Cumulative assessment

Daily assessment

Prevalence of infection (per 100,000)

Infected donations

Date

Date
Q fever outbreak in NL

Cumulative assessment

Daily assessment

Infected components

Infected products

Chronic infections in recipients
Conclusion

The EUFRAT can be used:

- to quantify the risk of emerging infections to blood safety
- to analyse the impact of preventive measures on transfusion safety
- to support decision making by public health policy makers (and transfusion regulators) in future
Project team

- Dr. Mart P. Janssen ~ TTA, Sanquin
- Dr. Cees L. van der Poel ~ TTA, Sanquin
- Dr. Mirjam Kretzschmar ~ UCID, RIVM
- Dr. Daniel Lewandowski ~ TTA
- Dr. Sybille Rehmet ~ ECDC
- Dr. Ardine de Wit ~ MTA, RIVM
- Dr. Jim van Steenbergen ~ CIb, RIVM
- Prof. Hans Zaaier ~ Sanquin, AMC
- Prof. Roel Coutinho ~ Julius Centre, RIVM
Questions and discussion