Worked-out examples of outbreak scenarios

This document contains two worked-out assessments of historical outbreaks that should provide guidance to the novel user of the *EUFRAT* tool to get familiarized with its use and various options.

Each of the examples starts with a description of the outbreak and a specification of various disease and donor population characteristics relevant to the modelling. Next, various analysis will be performed step by step. This should guide the novel user through various parts of the model and illustrate the capabilities of the tool.

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Example 1: Chikungunya outbreak in Réunion

Description of the outbreak

A massive epidemic of Chikungunya virus (CHIKV) occurred on Reunion Island during 2005-2007, having a serious impact on the local blood supply.[1] Over a period of 104 days, 6,864 cases of infected individuals were reported in a regional population of 757,000. Chikungunya infections are asymptomatic in an estimated 65.7% of cases.[1,2] Infected individuals are infectious from 1.5 days after getting infected and remain infectious for 7.5 days.[3] The proportion of chronic infections is 12.5%.[3] Chronic infections last for approximately 120 days and affected individuals remain infectious throughout this period. Donors are assumed to have a similar risk of getting infected as the general population as the disease is commonly transmitted by mosquito bites in the affected region. Therefore the relative risk of infection is 1 (RR=1). A Donor Health Questionnaire (DHQ) was available, which is presumed to be able to detect 70% of the acute infected and 10% of chronic infections. The effectiveness of this questionnaire is 80% which means that of all cases potentially identifiable it will still miss 20%. A stable donor population of 15,140 donors is presumed, who on average deliver 29,469 donations which are used to produce 29,217 red blood cells, 14,294 platelets and 35,339 FFP products annually. It is assumed that each of the components is equally likely to transmit infection, and that the production processes does not reduce infectivity. Also, there is no immunity against the disease among transfusion recipients. The estimated incidence of severe chikungunya virus infection is 2 per 1,000 infected individuals, the estimated mortality 1 per 1,000 infected individuals.[1,3]

Setting the basic model, selecting the analysis setting

Some disease-specific model parameters are already incorporated in the tool. To load these default values, select “Chikungunya” in specification question 1 (Q1). In this example we restrict the analysis to transfusion recipients in the outbreak area itself (Q2 set to ‘No’). As we want to consider a chronic phase and the impact of a donor health questionnaire we set Q4 and Q5 to ‘Yes’.

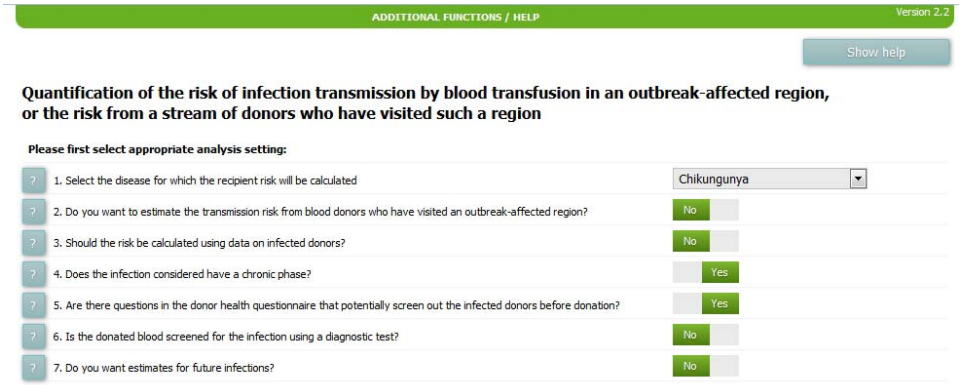


Figure 1.1 Loading background data and setting specification questions

As the appropriate analysis setting is selected now, the input values for various model parameters can be set. We will enter these per step.

Entering disease and outbreak data

Clicking the 'Expand' button of Step 1 will unfold the entries for 'Disease and Outbreak' model parameters (Figure 1.2). Note that data on disease-specific characteristics have indeed been loaded. However, in our assessment we want the duration of the acute infection to be 7.5 instead of 5 days. Also, the standard values for Population exposure & susceptibility need to be adjusted according to our requirements.

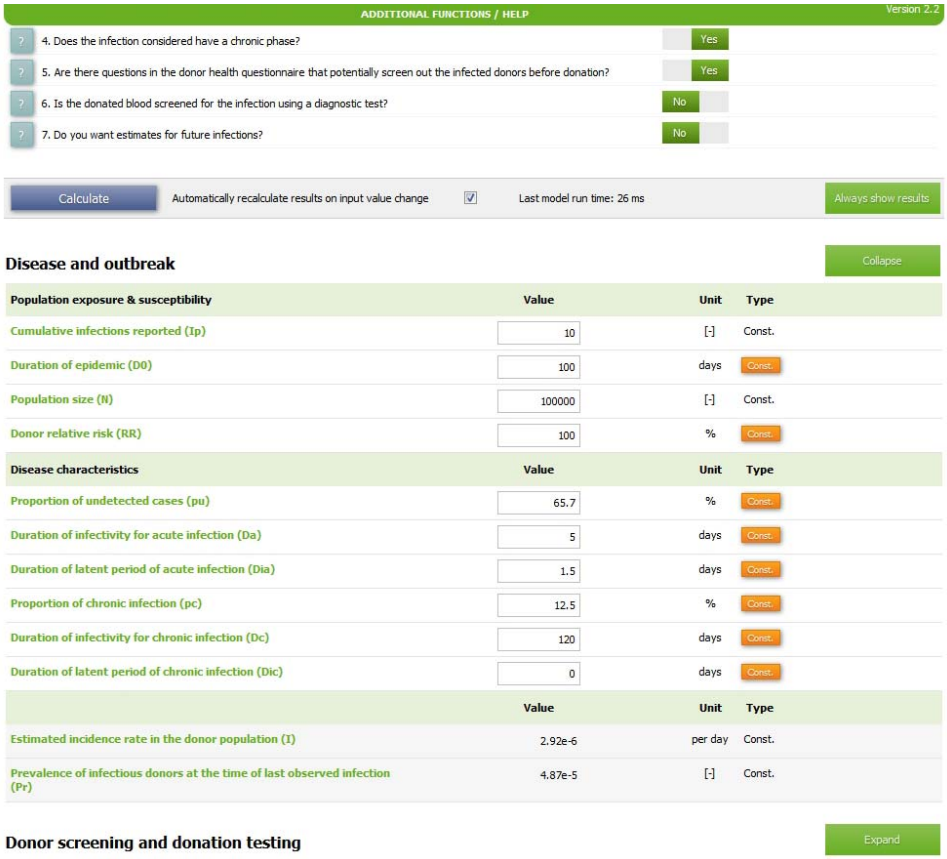


Figure 1.2: Showing Disease and outbreak data.

After changing 'Population exposure & susceptibility' parameters and the duration of the acute infection, new estimates for the prevalence and incidence for the donor population will be automatically calculated (Figure 1.3).

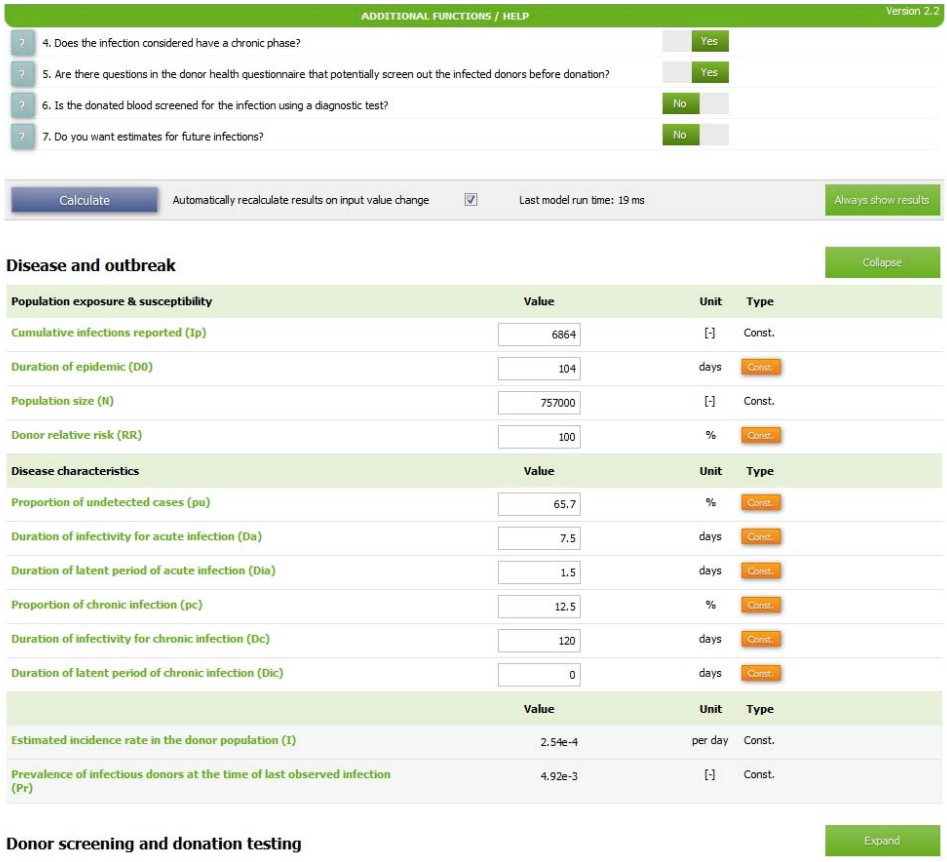


Figure 1.3: Changing Disease and outbreak data.

Entering screening and testing data

Now the donor screening and donation testing data can be entered. First click on the 'Collapse' button for Step 1 ('Disease and outbreak') and unhide the Step 2 input fields by clicking the Expand button for Step 2 ('Donor screening and donation testing'). After entering the appropriate values this step will provide an estimate for the prevalence of infectious donors after screening (see Figure 1.4 below).

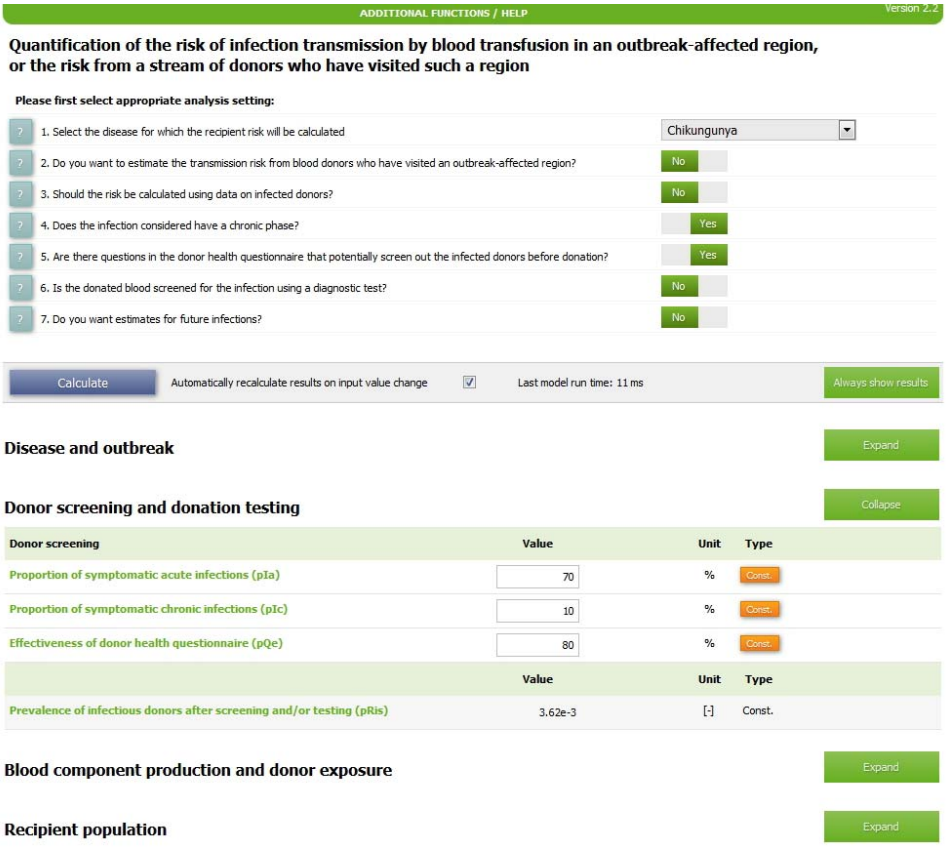


Figure 1.4: Changing Donor screening and donation testing data.

Entering data on component production and donor exposure

Next data on the production of blood components needs to be entered in order to determine the impact of the outbreak on the number of infected blood products transfused. Collapse Step 2 ('Donor screening and donation testing') and unhide the input fields for Step 3 by clicking its' Expand button ('Blood component production and donor exposure') (Figure 1.5).

Per type of donation an estimate of the number of products obtained from individual donations per year is required. Note that the number of products from individual donations that have *contributed* to the production of end products for transfusion are referred to, not the number of end products. For products that are obtained from pooling five donations, five times the number of end products should be entered here; for products that are split however, it is the actual number of end products that need to be entered instead of the number of individual donations.

After entering the appropriate values, this step will provide an estimate for the number of infected products per product type (see Figure 1.5 below). Because the entire donor population is exposed this setting does not require any changes.

Optionally, the table headers (product type names) can be changed by pressing <SHIFT> whilst clicking on the name of the product type.

Blood component production and donor exposure — Collapse

Type of donation	Number of donors	Number of products obtained from individual donations per year: Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Whole blood	15140	29217	14294	35339	0	[-]
Platelet pheresis	0	0	0	0	0	[-]
Plasmapheresis	0	0	0	0	0	[-]
Other donations	0	0	0	0	0	[-]
Total number of donors/products per year	15140.00	29217.00	14294.00	35339.00	0.00e+0	[-]

Number of donors exposed. Specify as:	Value	Unit	Type
Total number of donors	15140.00	[-]	Const.
Proportion of the total number of donors	10	%	Const.
Specified number of donors exposed	10000	[-]	Const.
Number of donors exposed (Ndo)	15140.00	[-]	Const.

Risk reduction	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Remaining risk of transmission after processing (pit)		100	100	100	100	%
Number of infected products (Nip)	97.65	36.18	17.70	43.77	0.00e+0	[-]

Recipient population — Expand

Figure 1.5: Changing Blood component production and donor exposure.

Entering recipient population characteristics

In the final step (Step 4, 'Recipient population') the impact of infected products on the recipient population is determined. With no immunity presumed, and a probability of severe infection of 0.002 and of death of 0.001 per infected individual, the total number of fatalities from transmissions by blood transfusion is calculated after entering these data (see Figure 1.6). There is a 0.1% probability that an individual will die from transmission through an infected blood component.

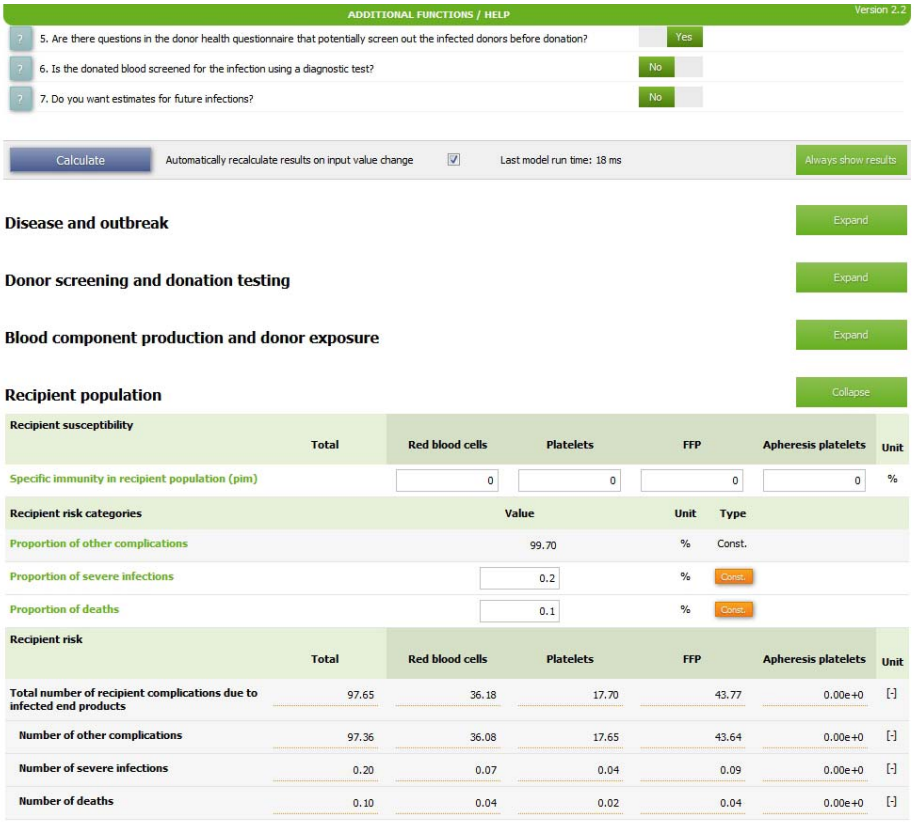


Figure 1.6: Estimated number of fatalities from blood transfusion by infected donors.

Assessing the impact of the donor questionnaire

The effectiveness of the donor health questionnaire can be easily assessed by simply setting the slide for question 5 (Q5) to 'No' (see Figure 1.7). From the reduction in the total number of complications it is clear that the reduction in the number of transmissions is around 30%.

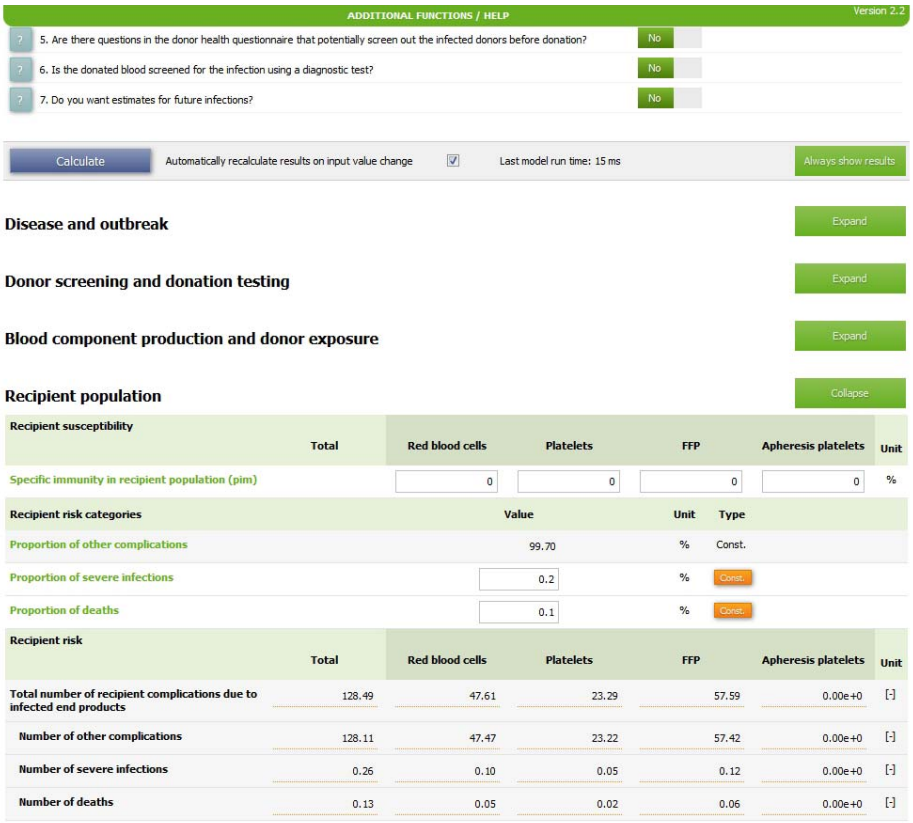


Figure 1.7: Estimated number of fatalities from blood transfusion by infected donors without donor screening.

Saving the input data and results for future reference

In order to allow reproduction of the results, the current inputs and outputs can be saved to an output file ('.CSV' text file). The output file can be used both for reading back in all currently used data and settings, and for post processing of the results.

The save/load functions are available on the 'Save/load' tab of the 'Additional functions / help' section which is accessible under the header bar of the *EUFRAT* tool (Figure 1.8).

Data are automatically stored in a file named 'EUFRAT_parameters.csv'.

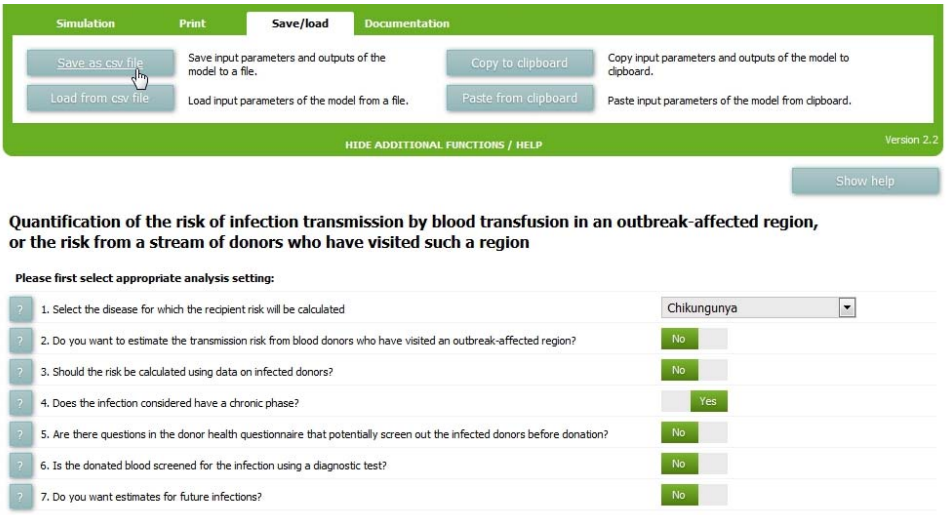


Figure 1.8: Save input data and results.

Assessing the impact of parameter uncertainty

By pressing the orange type indicator button of a model parameter its type can be changed from 'Constant' to 'Distributed'. For 'Distributed' model parameters, a range of values will be simulated to calculate the associated range of model output values.

Open the 'Disease and outbreak' input section by pressing the 'Expand' button, and set the ranges for the proportion of undetected cases to [50, 80], and duration of infectivity for acute infection to [2, 12] (Figure 1.9).

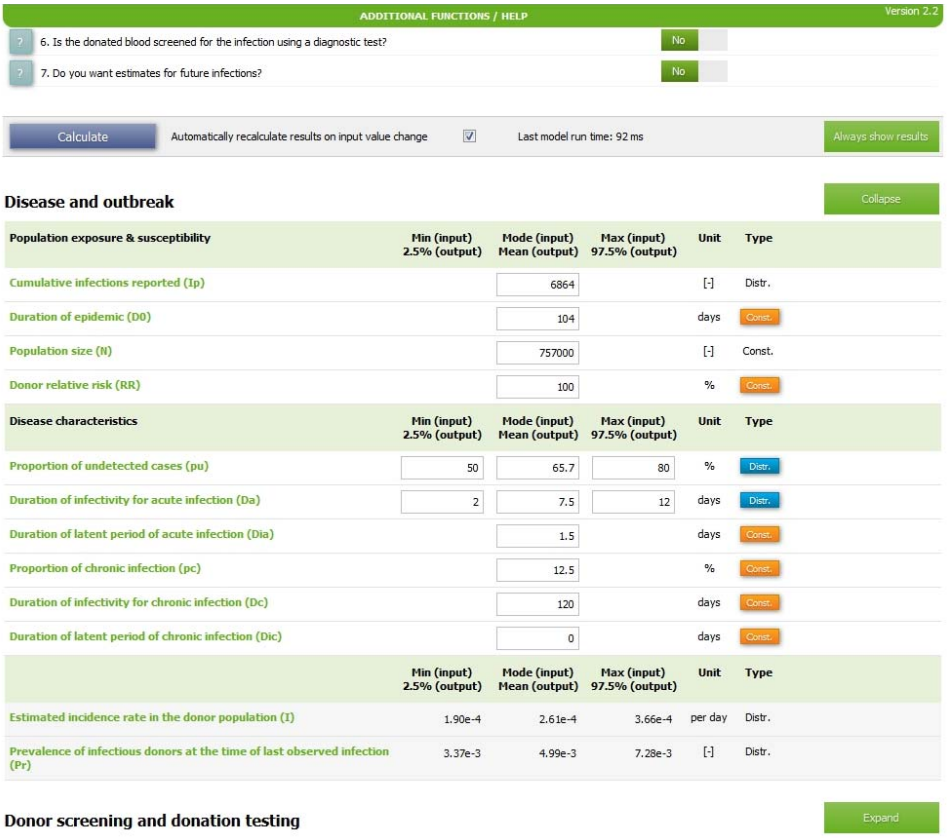


Figure 1.9: Setting model parameters to become 'Distributed' parameters.

The output of the model will not change (See Figures 1.7 and 1.10), but note that the dotted line underneath the outcomes has changed colour from orange to blue, indicating that these outcomes are the result of a simulation.

A mouse click on any number with a blue underlining will result in the popup of a window with an 'Info' and a 'Chart' tab. The chart tab shows the distribution of outputs for the set number of simulations. The accuracy of the simulated output can be increased by increasing the number of simulations. This is advisable in those cases where pressing the calculate button will result in a substantial change in output values.

Note that the 95% CI (the 2.5% and 97.5% percentile values, 87.31 and 193.03) are 32% lower and 50% higher than the mean value.

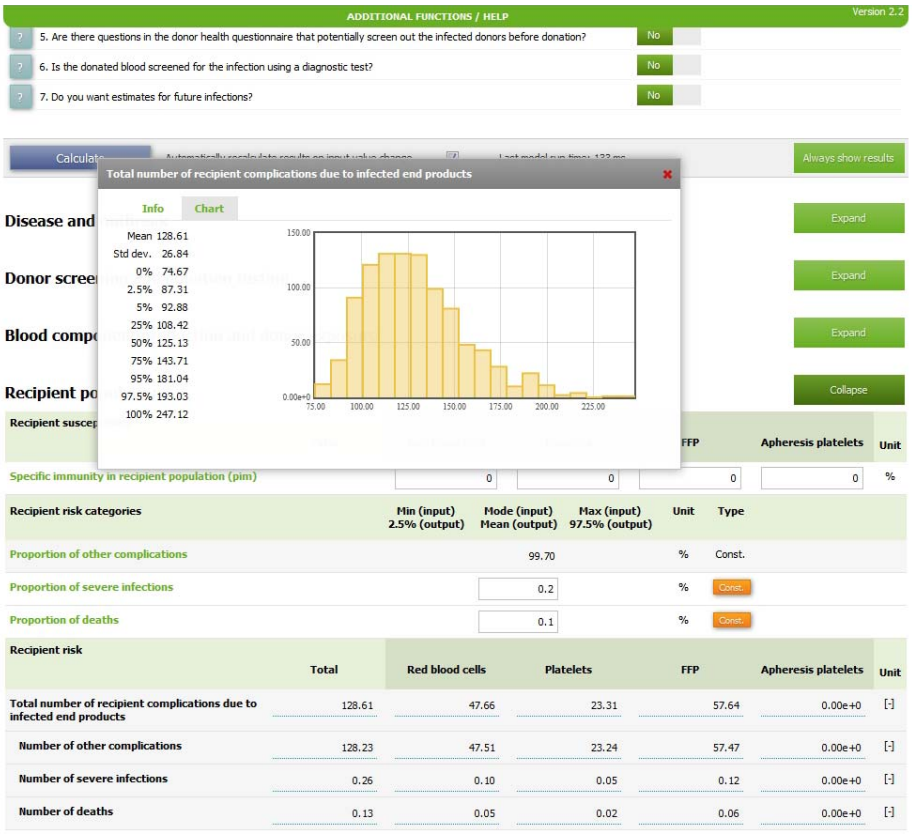


Figure 1.10: Viewing the distribution of model output values.

Due to the large number of infections observed in this example, the level of uncertainty in the outcome estimates is limited. But what if we would have observed only 7 infections in a population of 757 inhabitants?

The result is shown in Figure 1.11. Note that the point estimate has hardly changed (from 128.61 to 130.88, which is 2%), but the 95% CI has changed from [87.31, 193.03] to [45.79, 278.09], so to -64% and +116% which is around twice the level of uncertainty.

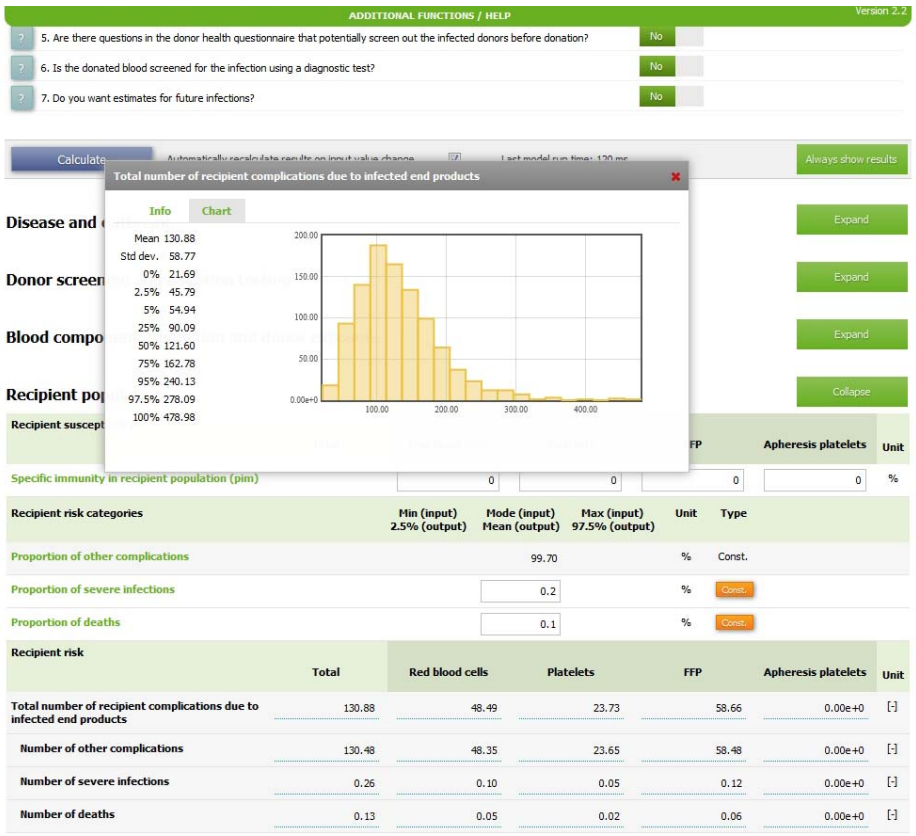


Figure 1.11: Increased uncertainty in model inputs.

Despite the fact that a random simulation process is applied it is possible to obtain reproducible model output. This is done by setting the 'Random number seed' value, which determines the starting point of the range of random numbers generated. The input for the seed value is provided in the 'Simulation' tab of the 'Additional functions / help' section which is accessible under the header bar of the *EUFRAT* tool (see Figure 1.12). A new calculation with 1000 samples will now lead to a mean estimate of 130.92 infections in total with a 95% CI of [45.61, 264.82]. Increasing the sample size to 100,000 will ensure a more robust estimate (Figure 1.13). Note however that increasing the number of samples will also increase calculation time considerably.

You can also monitor the impact of adding new samples by unchecking the 'Automatically recalculate results on input value change' checkbox to the right of the 'Calculate' button and unchecking the 'Repace samples' checkbox in the Simulation tab. You will now see the impact of adding new samples to the current result as the total number of samples will increase every time you press 'Calculate' (See Figure 1.14). This will allow you to assess the stability of the outcome presented. A good strategy is adding the same number of samples as you currently have, so doubling the total number of samples after each step. Usually selecting 1000 samples will provide a good balance between accuracy (of average values) and calculation speed. However, once final results are obtained, one could process the model with a larger number of samples. Using 100 000 samples will in most cases lead to sufficiently stable estimates for confidence intervals, which are most sensitive to the number of samples chosen.

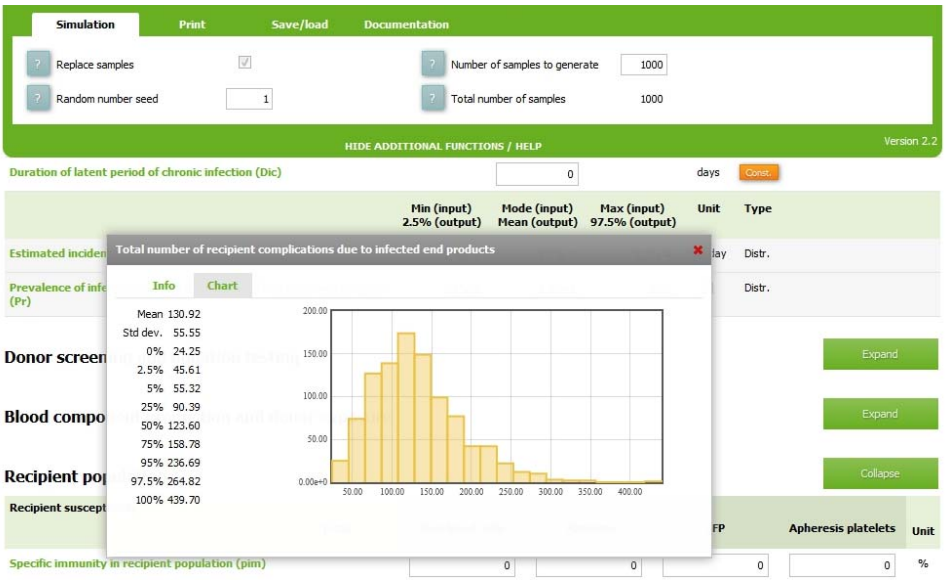


Figure 1.12: Setting a seed value.

Note that distributed outcomes may provide different results on different computers despite the setting of a random sample seed number.

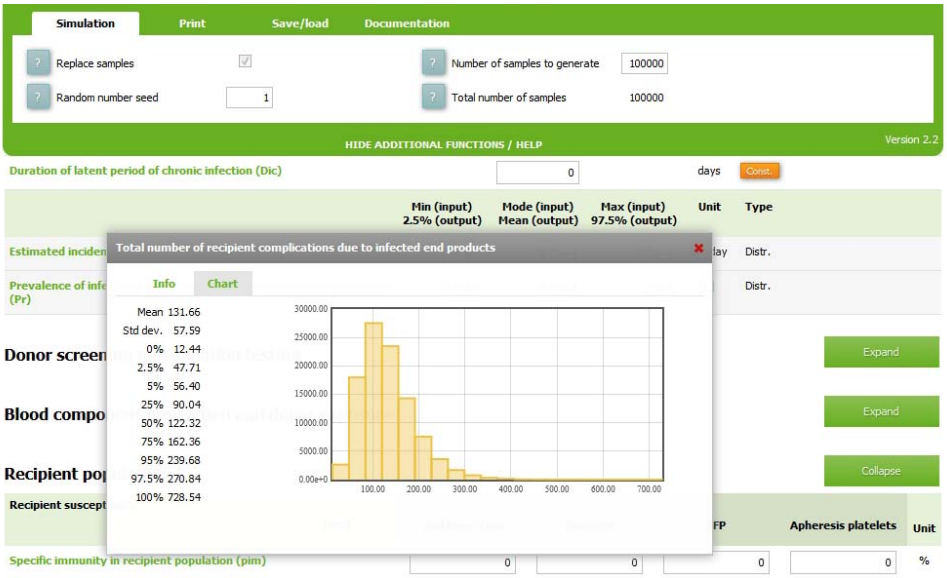


Figure 1.13: Setting a large sample number for robust estimates.

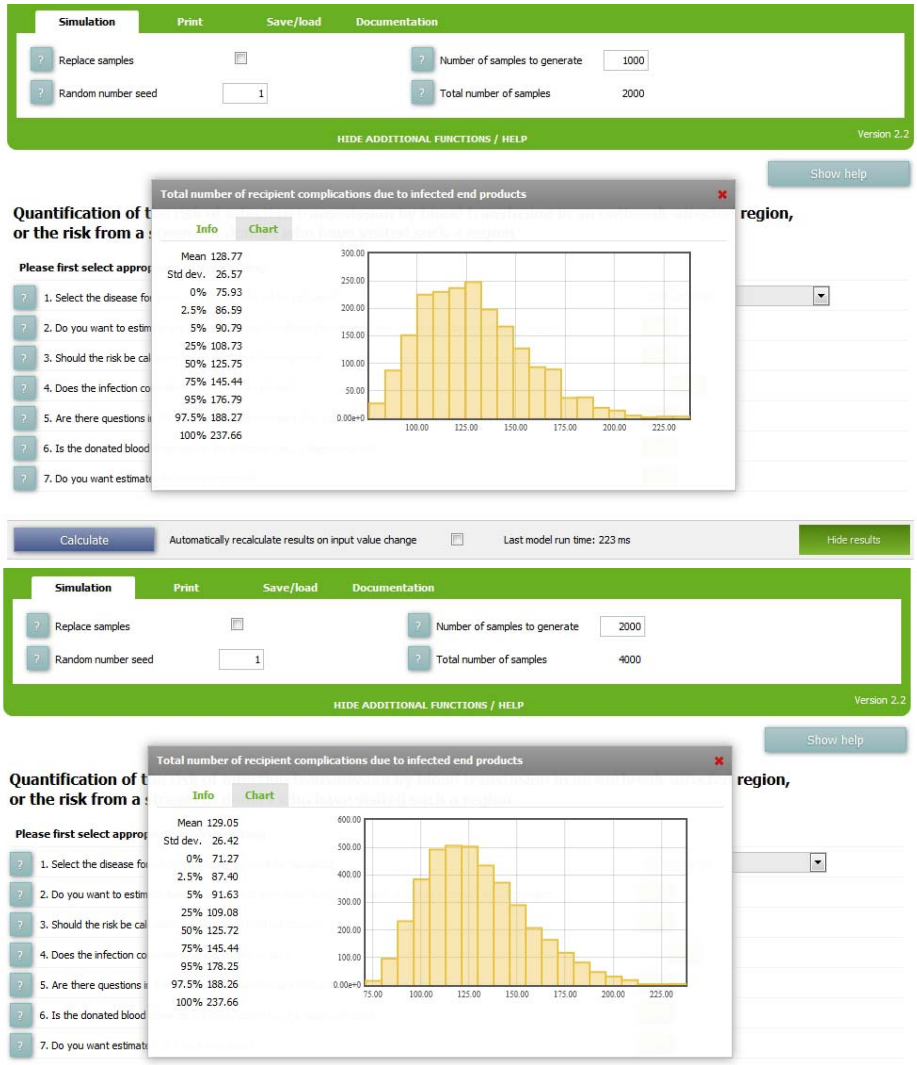


Figure 1.14: Stepwise increase of the number of samples to assess the stability of the risk estimates.

Assessing the risk from travelling donors

To assess the risk from donors who travelled to the outbreak area, first reset the number of simulations to avoid repetition of long calculation times. Next reset all model parameter values and set all parameter types to constant. You can also load the previously saved output file.

Now set the specification question Q2 to 'Yes', indicating that you want to estimate the transmission risk from blood donors who have visited an outbreak-affected region.

Next specify in Step 1 the newly added parameters which indicate the number of donor visits per day and their respective duration of stay. (see Figure 1.14 below).

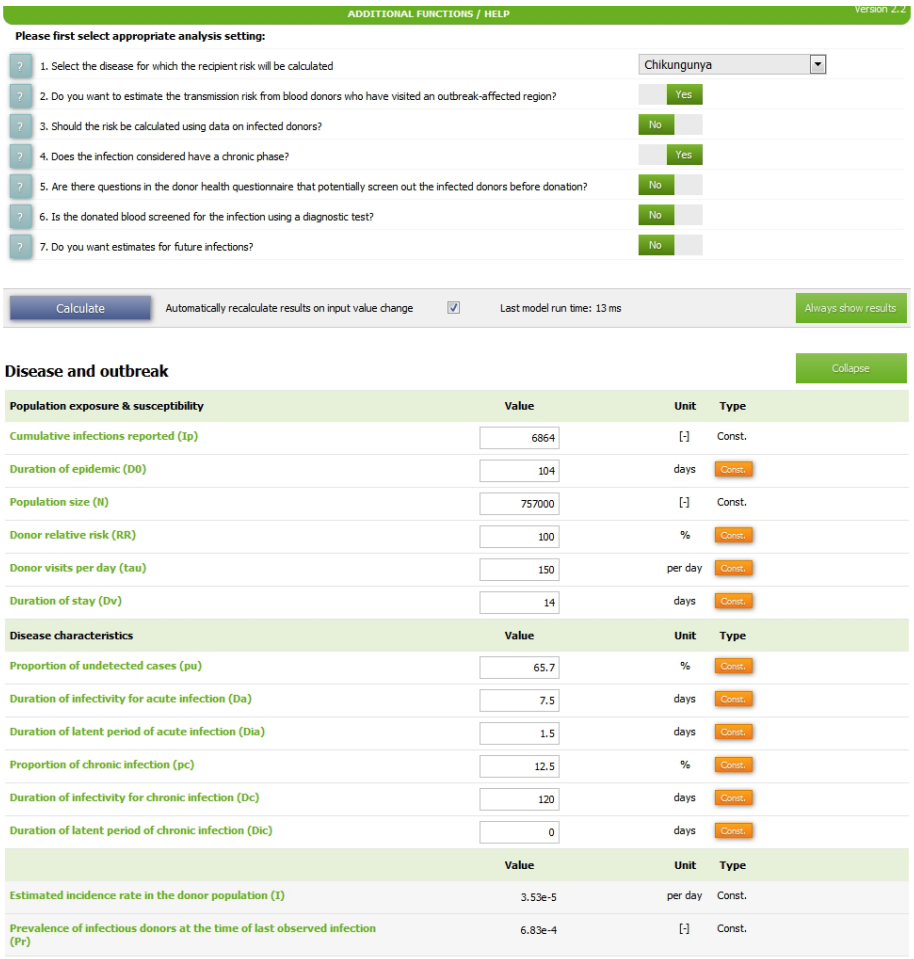
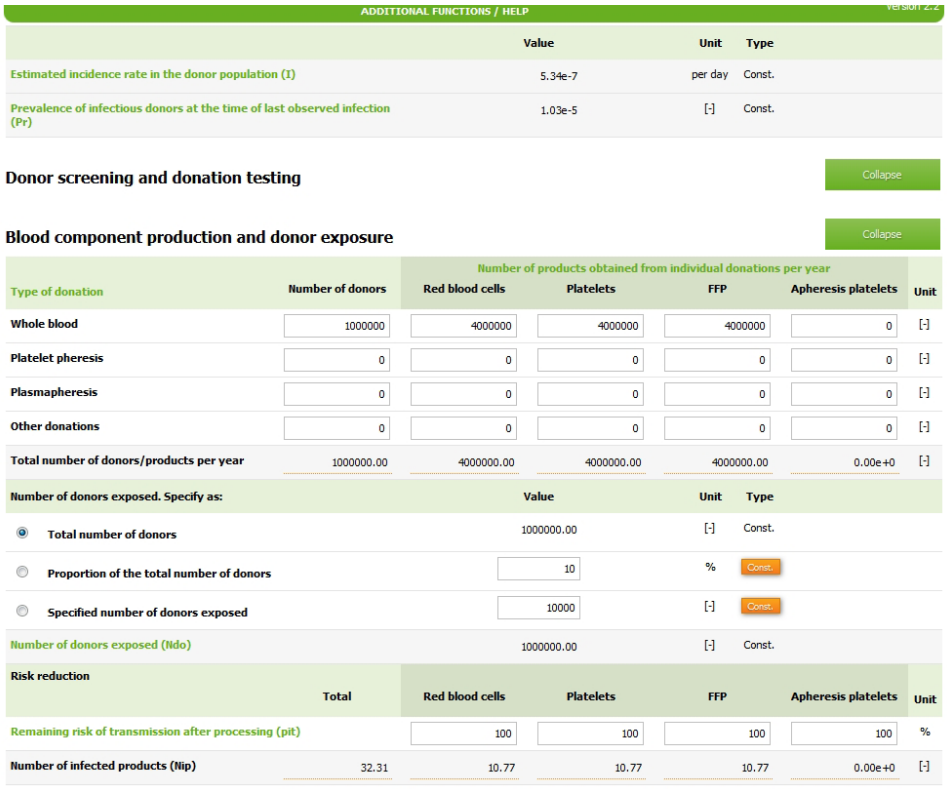


Figure 1.15: Setting model parameters for travelling donors.

In order to provide correct risk estimates the blood component production and donor exposure data have to be changed to reflect the characteristics of the country of residence of the donors. The size of the resident donor population is 1,000,000. Presume that these donors provide four whole blood donations per year which are 100% effectively used for the production of blood components, so resulting in 4,000,000 products for each product type. The number of infected products distributed is 32.

Note that changing the number of donors exposed does *not* affect this estimate: the number of infections transmitted is determined by the number of donors visiting and their duration of stay, and not by the size of the population that these donors originate from. The estimated incidence rate in the donor population and prevalence however *will* be affected by the number of donors exposed.



ADDITIONAL FUNCTIONS / HELP

	Value	Unit	Type
Estimated incidence rate in the donor population (I)	5.34e-7	per day	Const.
Prevalence of infectious donors at the time of last observed infection (Pr)	1.03e-5	[-]	Const.

Donor screening and donation testing Collapse

Blood component production and donor exposure Collapse

Type of donation	Number of donors	Number of products obtained from individual donations per year: Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Whole blood	1000000	4000000	4000000	4000000	0	[-]
Platelet pheresis	0	0	0	0	0	[-]
Plasmapheresis	0	0	0	0	0	[-]
Other donations	0	0	0	0	0	[-]
Total number of donors/products per year	1000000.00	4000000.00	4000000.00	4000000.00	0.00e+0	[-]

Number of donors exposed. Specify as:	Value	Unit	Type
Total number of donors	1000000.00	[-]	Const.
Proportion of the total number of donors	10	%	Const.
Specified number of donors exposed	10000	[-]	Const.
Number of donors exposed (Ndo)	1000000.00	[-]	Const.

Risk reduction	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Remaining risk of transmission after processing (pit)		100	100	100	100	%
Number of infected products (Nip)	32.31	10.77	10.77	10.77	0.00e+0	[-]

Figure 1.16: Travelling donor country of residence donation characteristics.

Future infections

To assess the risk from donors who travelled to the outbreak area, first reset the number of simulations to avoid repetition of long calculation times. Next reset all model parameter values and set all parameter types to constant. You can also load the previously saved output file which will reset all model parameters and settings those of the original Chikungunya outbreak.

Set the specification question Q7 to 'Yes', indicating that you want estimates for future infections. What you will see is that two new blue bars will appear in Step 1: The first is the input value of the time point for evaluating of the future risk (*Tx*). The second is the estimated prevalence at time *Tx*. By changing the time point *Tx*, the prevalence at any point in time can be calculated. Note that the prevalence estimate provided is the prevalence of both acute *and* of chronic infections (Figure 1.17).

For the steps 3 and 4, where the number of infected products and the number of recipient complications are calculated, additional results are provided in blue, including estimates for the number of infected products and infections in recipients that will occur after time point *Tx* (see also Figure 1.18).

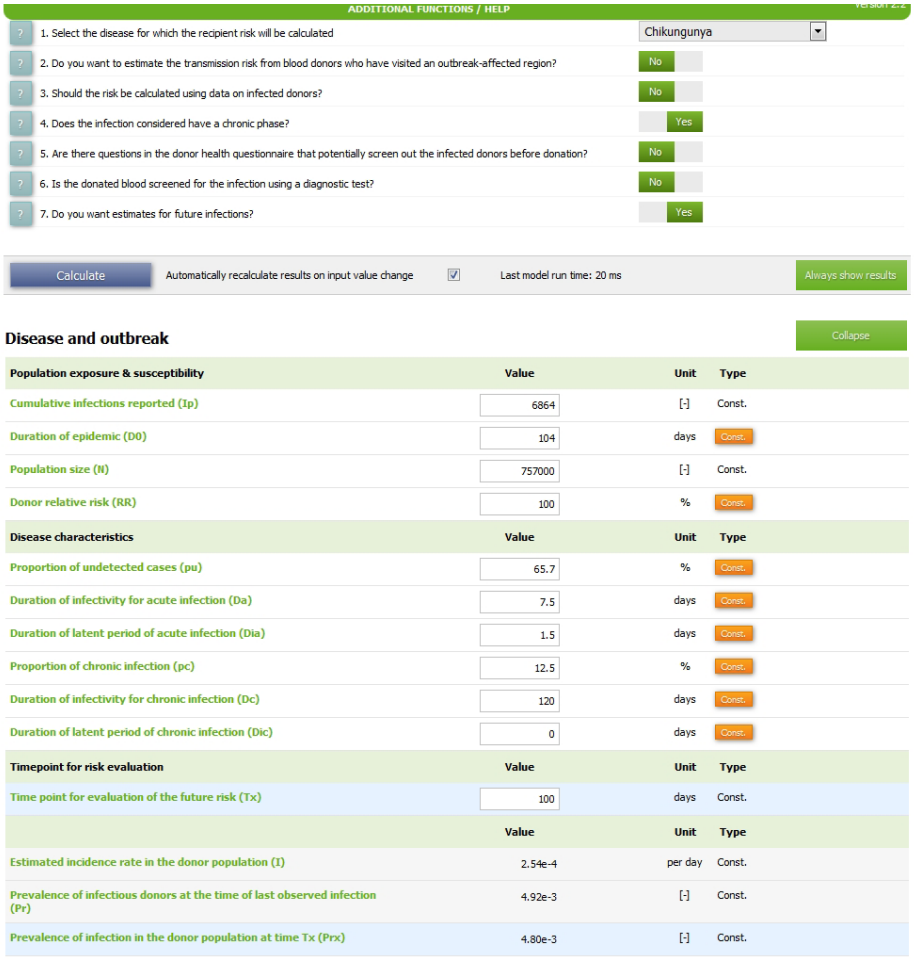


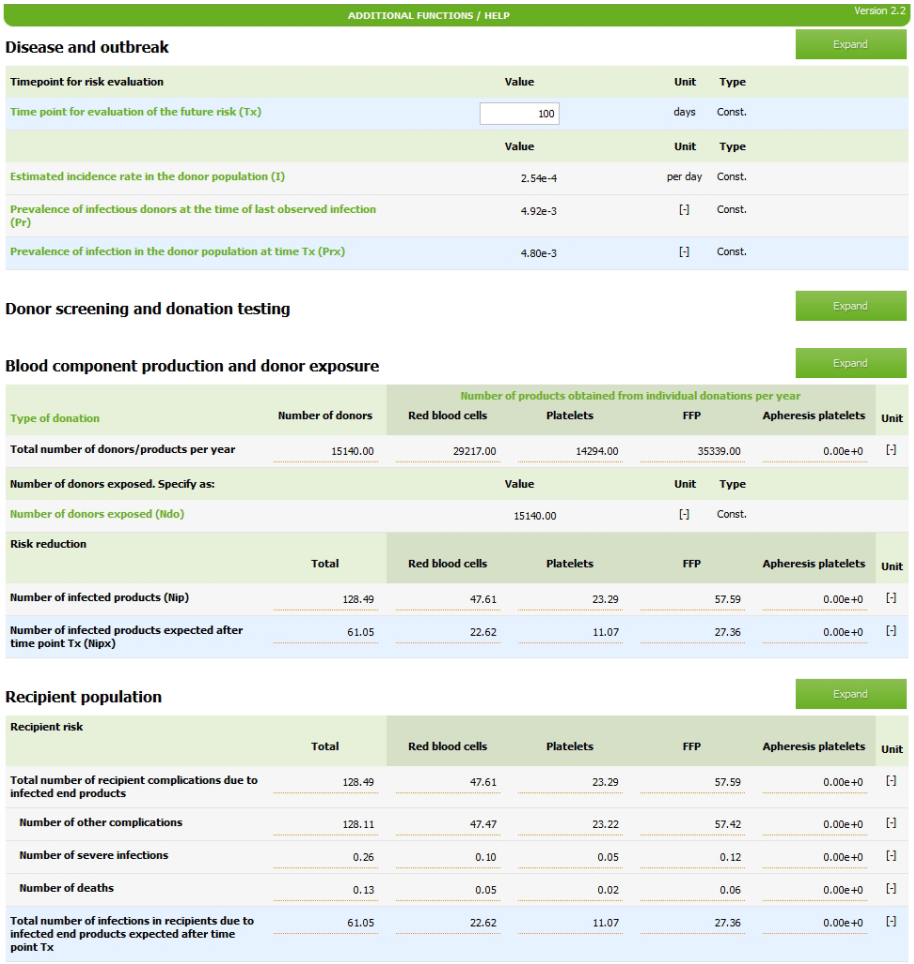
Figure 1.17: Calculating future infections.

Always showing results

When the 'Always show results' button opposite the 'Calculate' button is pressed, all calculated results will show irrespective of the status of the Expand/Collapse button of each Step. In addition, if the user has selected calculation of future risks (Q7), the time point for evaluating of the future risk (*Tx*) will remain visible as well as all risk estimates for this time point (See Figure1.18). This allows continuous viewing of the outputs, possibly whilst toggling or changing model setting or model parameter input.

To hide the results just press the same button, which is now labelled 'Hide results'.

Note that for the Chikungunya outbreak almost half the infection transmissions are expected to occur after the end of the outbreak.



ADDITIONAL FUNCTIONS / HELP — Version 2.2

Disease and outbreak — Expand

Timepoint for risk evaluation	Value	Unit	Type
Time point for evaluation of the future risk (Tx)	100	days	Const.

	Value	Unit	Type
Estimated incidence rate in the donor population (I)	2.54e-4	per day	Const.
Prevalence of infectious donors at the time of last observed infection (Pr)	4.92e-3	[-]	Const.
Prevalence of infection in the donor population at time Tx (Prx)	4.80e-3	[-]	Const.

Donor screening and donation testing — Expand

Blood component production and donor exposure — Expand

Type of donation	Number of donors	Number of products obtained from individual donations per year: Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Total number of donors/products per year	15140.00	29217.00	14294.00	35339.00	0.00e+0	[-]

Number of donors exposed. Specify as:	Value	Unit	Type
Number of donors exposed (Ndo)	15140.00	[-]	Const.

Risk reduction	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Number of infected products (Nip)	128.49	47.61	23.29	57.59	0.00e+0	[-]
Number of infected products expected after time point Tx (Nipx)	61.05	22.62	11.07	27.36	0.00e+0	[-]

Recipient population — Expand

Recipient risk	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Total number of recipient complications due to infected end products	128.49	47.61	23.29	57.59	0.00e+0	[-]
Number of other complications	128.11	47.47	23.22	57.42	0.00e+0	[-]
Number of severe infections	0.26	0.10	0.05	0.12	0.00e+0	[-]
Number of deaths	0.13	0.05	0.02	0.06	0.00e+0	[-]
Total number of infections in recipients due to infected end products expected after time point Tx	61.05	22.62	11.07	27.36	0.00e+0	[-]

Figure 1.18: Showing all model outputs.

Example 2: West Nile Virus outbreaks in Northern Italy

Description of the current situation

The recurrence of WNV outbreaks in several EU member states instigates the assessment of the risk of local travelling donors. Italy is a popular holiday destination that is also confronted with WNV outbreaks during the summer holiday peak season. A seroprevalence as high as 0.01 (44 reactive in 4450 tested) amongst blood donors has been recorded.[4] In 2013 a total of 20 confirmed cases of West Nile Neuroinvasive Disease (WNND) were recorded in the Emilia-Romagna region.[5] This region has 4,446,354 inhabitants. Between 2,000 and 3,000 donors from the Netherlands visited this region during the outbreak season (June-October, 4 months, so 17-25 donors per day), who on average stay there for 14 days.[6]

The Dutch donor population consists of 363,878 whole blood repeat donors. These donors deliver 428,245 red blood cells, 262,848 platelet units (from donations), and 55,056 FFP units for transfusion. Presume that there is no reduction in infectivity in the production process.

The vast majority of infections are asymptomatic (80%).[7] The duration of the acute infectivity is known to be 6 days (range 1-11 days) with an incubation time of 1 to 2 days.[7,8] There is no chronic infection. Studies show that around 1% of infections have a severe manifestation (West Nile Neuroinvasive Disease WNND) and that the mortality rate of WNND is 10%.[7]

Setting the basic model, selecting the analysis setting

Some disease specific model parameters are already incorporated in the tool. To load these default values, select “West Nile virus infection” in specification question 1 (Q1). As we want to assess the risk from travelling donors, the answer to the second question is ‘Yes’. All other questions remain in the ‘No’ position (Figure 2.1).

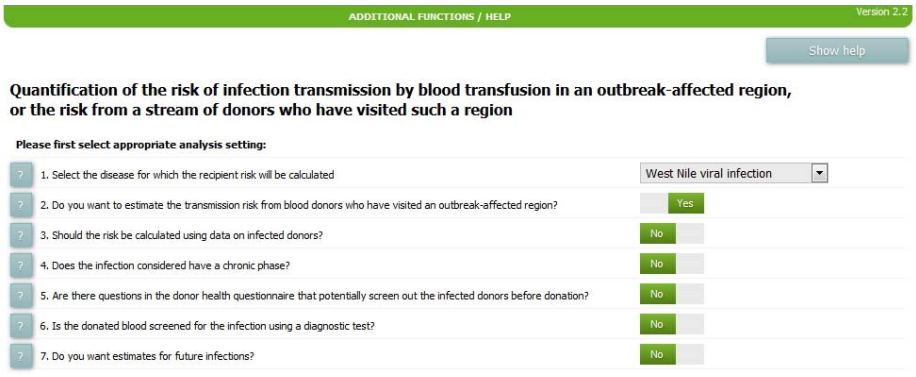


Figure 2.1: Loading background data and setting specification questions

As the appropriate analysis setting is selected now, the input values for various model parameters can be set. We will enter these per step.

Entering disease and outbreak data

Clicking the 'Expand' button of Step 1 will unfold the entries for 'Disease and Outbreak' model parameters (Figure 2.2). Note that data on disease specific characteristics have indeed been loaded. Note that the disease characteristics are correct for our analysis, but the 'Population exposure & susceptibility' parameters need to be adjusted according to our requirements. Also, if we presume that only 1% of the WNV infections lead to WNND disease, then we should model that the proportion of undetected cases is 99%.
We presume that the relative risk for visitors is the same as for local residents. Note that because no information is provided on the donor population in the Netherlands, the incidence and prevalence cannot be calculated yet.

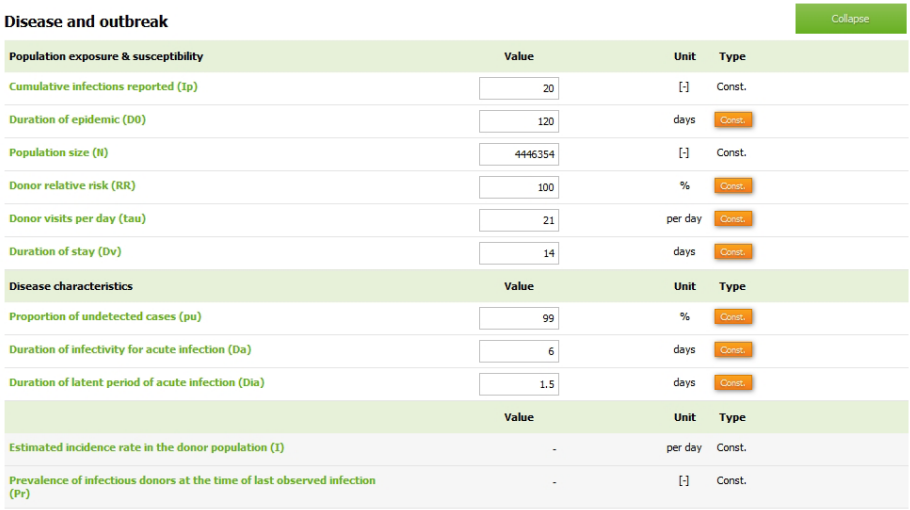
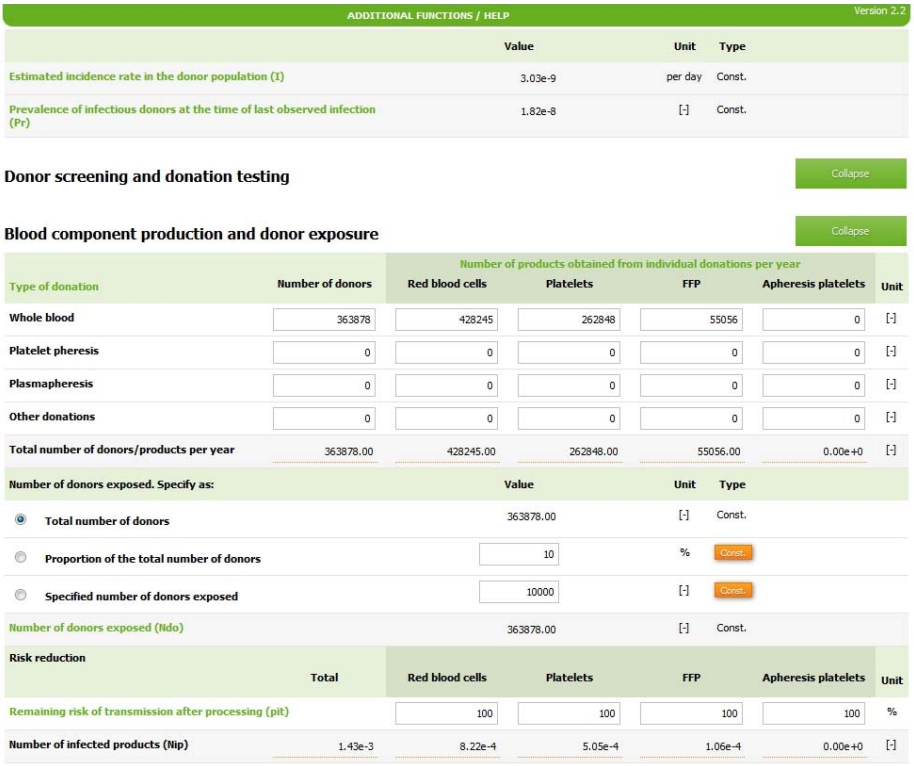


Figure 2.2: Entering Disease and outbreak data.

Entering data on blood component delivery and donor exposure

These numbers can be directly copied from the data provided in the case description: 363,878 whole blood repeat donors, 428,245 red blood cells, 262,848 platelet units (from donations), and 55,056 FFP units.
After entering these values the output for this step provides an estimate of the number of infected products per product type (see Figure below). Also, now that the size of the donor population is known, the incidence in the donor population (output of step 1, also shown in Figure 2.3) and the prevalence at the end of the outbreak period are provided.

The table headers (product type names) can be changed by pressing <SHIFT> whilst clicking on the name of the product type.



ADDITIONAL FUNCTIONS / HELP — Version 2.2

	Value	Unit	Type
Estimated incidence rate in the donor population (I)	3.03e-9	per day	Const.
Prevalence of infectious donors at the time of last observed infection (Pr)	1.82e-8	[-]	Const.

Donor screening and donation testing — Collapse

Blood component production and donor exposure — Collapse

Type of donation	Number of donors	Number of products obtained from individual donations per year: Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Whole blood	363878	428245	262848	55056	0	[-]
Platelet pheresis	0	0	0	0	0	[-]
Plasmapheresis	0	0	0	0	0	[-]
Other donations	0	0	0	0	0	[-]
Total number of donors/products per year	363878.00	428245.00	262848.00	55056.00	0.00e+0	[-]

Number of donors exposed. Specify as:	Value	Unit	Type
(•) Total number of donors	363878.00	[-]	Const.
( ) Proportion of the total number of donors	10	%	Const.
( ) Specified number of donors exposed	10000	[-]	Const.
Number of donors exposed (Ndo)	363878.00	[-]	Const.

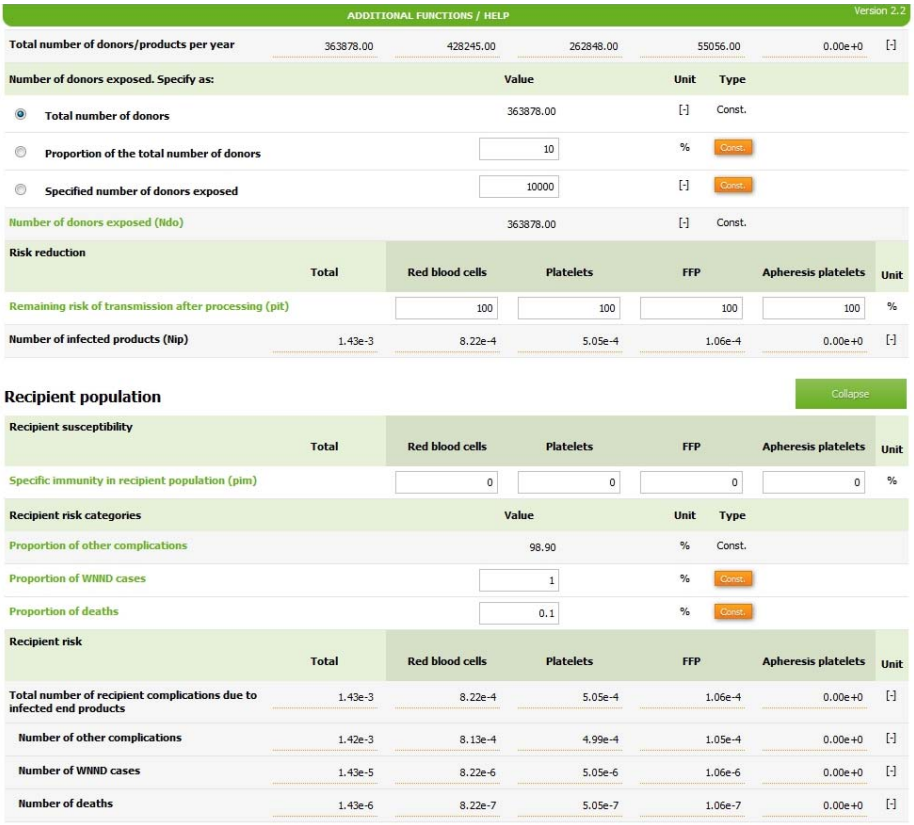
Risk reduction	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Remaining risk of transmission after processing (pit)		100	100	100	100	%
Number of infected products (Nip)	1.43e-3	8.22e-4	5.05e-4	1.06e-4	0.00e+0	[-]

Figure 2.3: Changing Blood component production and donor exposure.

From the output it can be found that 0.00143 infected products are expected. After entering the recipient complication probabilities the overall outcome will be calculated.

Entering recipient population characteristics

In the final step (Step 4, 'Recipient population') the impact of infected products on the recipient population is calculated. With no immunity presumed, and a probability of severe infection of 1% and of death of 0.1% per infected individual, the total number of fatalities from transmissions by blood transfusion is calculated. Note that the data that are loaded when selecting the West Nile virus infection match those of our assessment. (see Figure 2.4).



ADDITIONAL FUNCTIONS / HELP — Version 2.2

Total number of donors/products per year	363878.00	428245.00	262848.00	55056.00	0.00e+0 [-]

Number of donors exposed. Specify as:	Value	Unit	Type
Total number of donors	363878.00	[-]	Const.
Proportion of the total number of donors	10	%	Const.
Specified number of donors exposed	10000	[-]	Const.
Number of donors exposed (Ndo)	363878.00	[-]	Const.

Risk reduction	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Remaining risk of transmission after processing (pit)		100	100	100	100	%
Number of infected products (Nip)	1.43e-3	8.22e-4	5.05e-4	1.06e-4	0.00e+0	[-]

Recipient population — Collapse

Recipient susceptibility	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Specific immunity in recipient population (pim)		0	0	0	0	%

Recipient risk categories	Value	Unit	Type
Proportion of other complications	98.90	%	Const.
Proportion of WNND cases	1	%	Const.
Proportion of deaths	0.1	%	Const.

Recipient risk	Total	Red blood cells	Platelets	FFP	Apheresis platelets	Unit
Total number of recipient complications due to infected end products	1.43e-3	8.22e-4	5.05e-4	1.06e-4	0.00e+0	[-]
Number of other complications	1.42e-3	8.13e-4	4.99e-4	1.05e-4	0.00e+0	[-]
Number of WNND cases	1.43e-5	8.22e-6	5.05e-6	1.06e-6	0.00e+0	[-]
Number of deaths	1.43e-6	8.22e-7	5.05e-7	1.06e-7	0.00e+0	[-]

Figure 2.4: Estimated number of fatalities from blood transfusion by infected donors.

It is therefore expected that in the Netherlands a WNV transmission by blood transfusion from donors travelling to Northern Italy would occur once every 700 years. This would lead to one case of WNND every 70,000 years and one death on average every 700,000 years.

Assessing the impact of model parameter uncertainty

To address the impact of uncertainty, the model output is calculated for a range of parameter values for various parameters. There are between 17 and 25 travelling donors per day. Presume the number of undetected cases to lie between 98% and 99.9%, the duration of infection to range between 1 and 11 days, and the duration of latent infection to range between 1 and 2 days. The adapted input values for Step 1 are shown in Figure 2.5, the corresponding model output in Figure 2.6.

Note that the incorporating the uncertainty in model parameters has increased the estimated mean number of infection transmissions by 30%. However, as the new estimate becomes highly skewed, a much higher number of cases might occur. In the 'worst foreseeable case' (the 95% upper bound estimate) one case of WNND might occur every 16,825 years and one death on average every 168,252 years, which is an increase of 315% ($5.94x10^{-5}/1.43x10^{-5}$-1) as compared to the first estimate which didn't take model parameter uncertainty into account.

Disease and outbreak Collapse

Population exposure & susceptibility	Min (input) 2.5% (output)	Mode (input) Mean (output)	Max (input) 97.5% (output)	Unit	Type
Cumulative infections reported (Ip)		20		[-]	Distr.
Duration of epidemic (D0)		120		days	Const.
Population size (N)		4446354		[-]	Const.
Donor relative risk (RR)		100		%	Const.
Donor visits per day (tau)	17	21	25	per day	Distr.
Duration of stay (Dv)		14		days	Const.
Disease characteristics	**Min (input) 2.5% (output)**	**Mode (input) Mean (output)**	**Max (input) 97.5% (output)**	**Unit**	**Type**
Proportion of undetected cases (pu)	98	99	99.9	%	Distr.
Duration of infectivity for acute infection (Da)	1	6	11	days	Distr.
Duration of latent period of acute infection (Dia)	1	1.5	2	days	Distr.
	Min (input) 2.5% (output)	**Mode (input) Mean (output)**	**Max (input) 97.5% (output)**	**Unit**	**Type**
Estimated incidence rate in the donor population (I)	1.36e-9	3.67e-9	9.85e-9	per day	Distr.
Prevalence of infectious donors at the time of last observed infection (Pr)	5.18e-9	2.19e-8	6.30e-8	[-]	Distr.

Figure 2.5: Input for the uncertainty assessment.

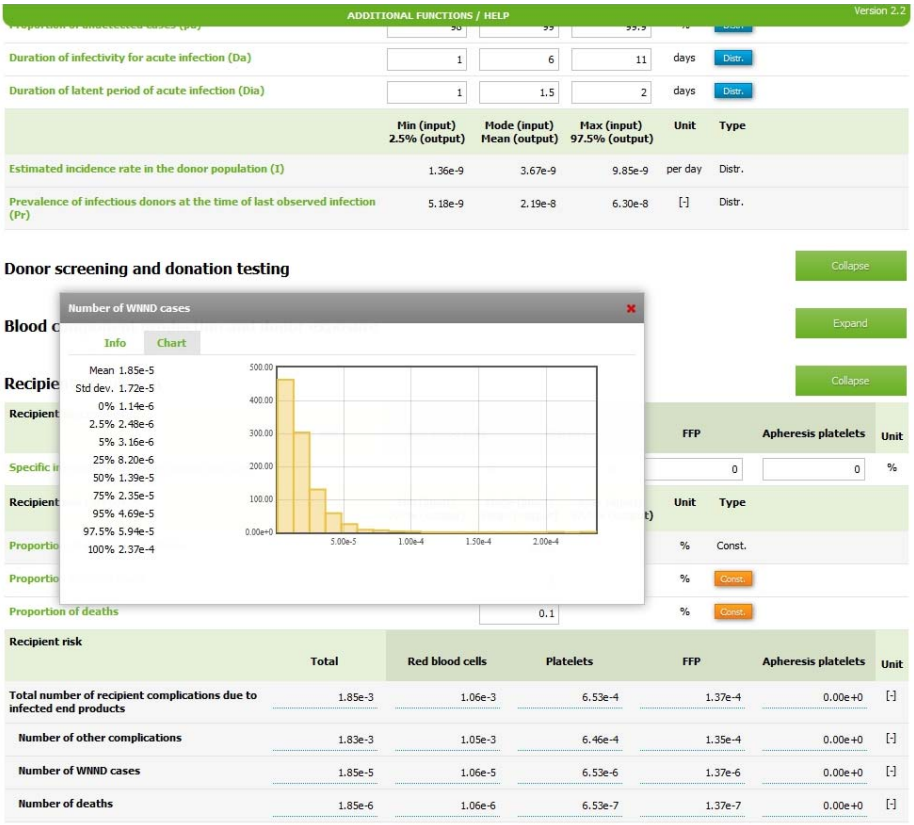


Figure 2.5: Output for the uncertainty assessment.

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