

– USER MANUAL – for the WHO RISK BASED DECISION SUPPORT TOOL FOR BLOOD SAFETY

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This manual is intended as a reference for users of the “*WHO risk based decision support tool for blood safety*”. This tool is provided as an Excel workbook containing a set of worksheets that will help the user to organize and prioritize various decision alternatives.

The tool allows assessing different interventions for blood safety and will provide estimates for a set of predefined outcomes for each of these options. Next, the optimal safety intervention can be derived by using a multiple criteria decision analysis, or by a qualitative assessment. For more information regarding both approaches and the use of the tool in general, we refer to the **User Guide** and the **Case Study** documents.

A risk based decision-making assessment requires different steps (Figure 1). The function of each of the steps in this process is explained in detail in the User Guide. This user manual focusses purely on the operation of the Excel workbook itself and explains the functions of various buttons and options. Throughout this document, screenshots of the tool are shown with text boxes explaining their respective functions and interpretation.

Note that the Excel workbook works best under MS Windows and does not work well on Apple computers. The tool was tested for Excel versions 2016 and 365.

If you have any questions or suggestions concerning the tool or the approach presented, please contact Mart Janssen, PhD, from Sanquin Blood Supply Foundation at m.janssen@sanquin.nl.

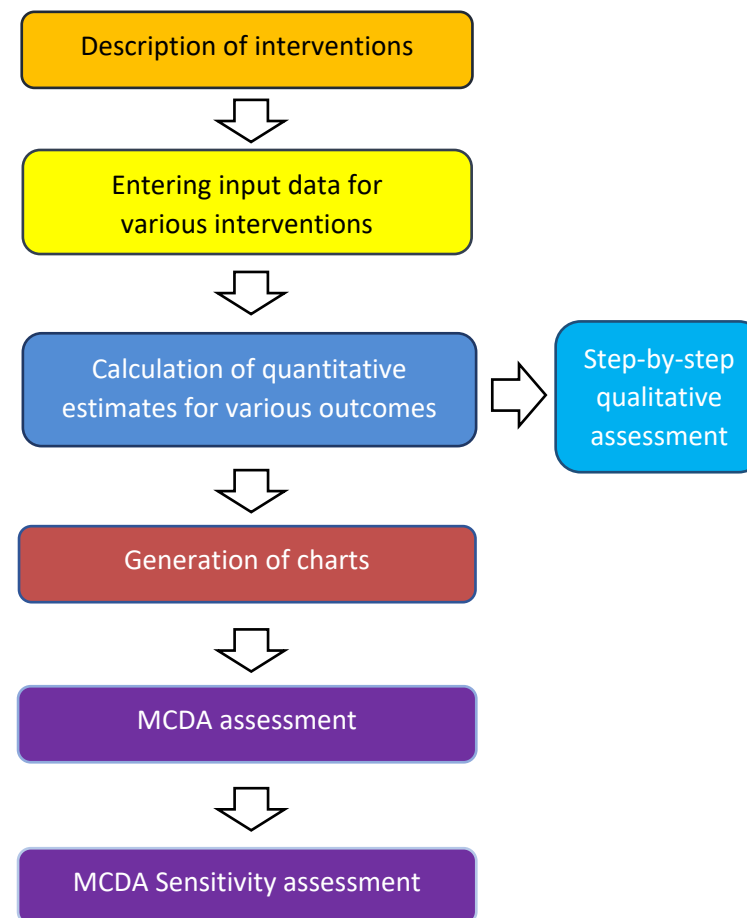


Figure 1 Steps in a risk based decision-making assessment

1. Description of interventions

1.1 On this worksheet, the user can elaborate a description of various safety interventions and associated outcomes and can add comments for each one of the combinations. The outcomes are defined in terms of (total) costs, number of deaths (prevented), number of blood products lost, and technological complexity of the safety intervention considered.

Enter the expected outcomes

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented
No testing	Baseline situation where no testing is performed	The cost of treatment of patients due to lack of preventive measures	Number of deaths given the number of infected products transmitted to
Rapid serologic testing	Screening of all or part of all blood donations	Costs of screening plus costs of treatment of infected patients	Idem

Enter a description for each of the outcomes

Enter a specific description for the outcome for the specific safety intervention

Enter a description for each one of the safety interventions

Note: The first two outcome columns are presumed to contain outcomes for total costs and fatalities. The last column reflects the cost-effectiveness ratio for each option based on these total costs and annual number of deaths.

Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity	Cost-effectiveness [US\$ per death prevented]
Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	The technological requirements considering education of personnel and availability of materials and support. These affect the overall effectiveness of the intervention	Total net cost per additional number of deaths prevented. This provides an indication of the "value for money" of the intervention relative to the baseline situation

Enter in the first 2 columns the main outcomes in terms of costs and fatalities

Cost-effectiveness of each safety intervention based on changes in total net costs and annual number of deaths

Note: The outcomes of the first safety intervention are used as a reference for the cost-effectiveness estimates for all other options considered.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity	Cost-effectiveness [US\$ per death prevented]
No testing	Baseline situation where no testing is performed	The cost of treatment of patients due to lack of preventive measures	Number of deaths given the number of infected products transmitted to	No costs	No screening implies that no products are lost	Not applicable	Comparator intervention and therefore not applicable

Reference values for the cost-effectiveness estimates of all alternative risk management options

1.2 All data input cells have a yellow fill color (background color) to facilitate identification. The yellow color can be shown or hidden by pressing the "show/hide input cells" button. This will change the fill color of the input cells in **ALL** the worksheets from the workbook to either be distinct (yellow) or look identical to all other cells.

Risk management strategy assessment for:

HIV screening of blood products

Hide input cells

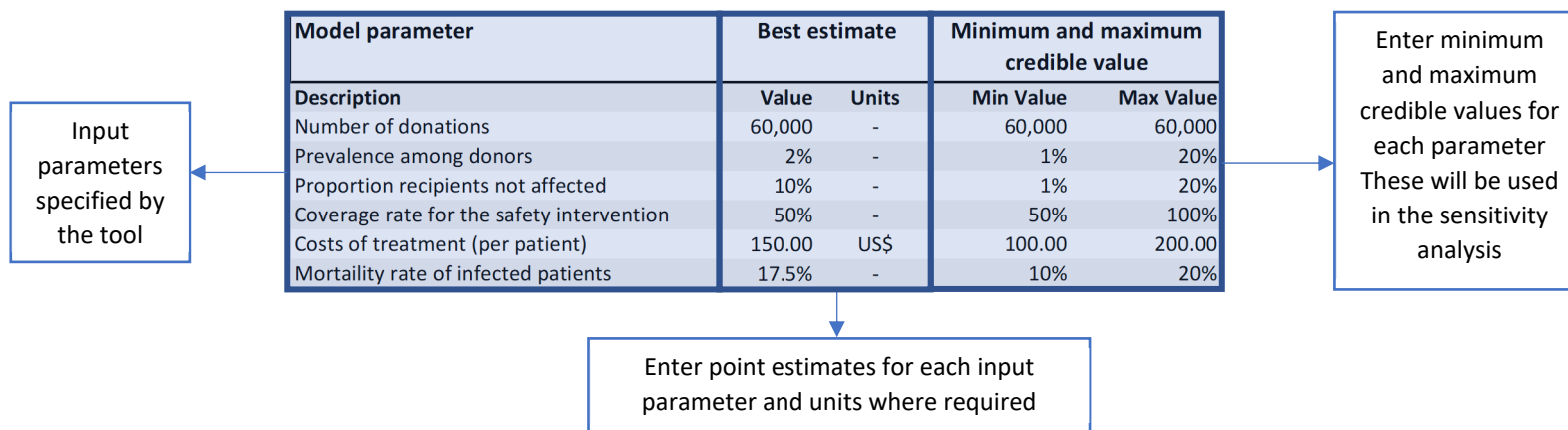
Press to toggle between a white (hidden) or yellow (discernable) background color for input cells

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented
No testing	Baseline situation where no testing is performed	The cost of treatment of patients due to lack of preventive measures	Number of deaths given the number of infected products transmitted to

Input cells shown in yellow

2. Entering input data for various interventions

2.1 For the calculation of various outcomes, common as well as specific input parameters per safety intervention are used. The model parameters are predefined in the tool. For each of the model input parameters, the user is required to enter an appropriate point estimate as well as and minimum and maximum credible values, and units if applicable.



3. Quantitative estimates for various outcomes

3.1 The input values entered in step 2.1 are used to calculate respective estimates for various outcomes per safety intervention considered.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	The technological requirements considering education of personnel and availability of materials and support. These affect the overall effectiveness of the intervention
No testing	Baseline situation where no testing is performed	162,000	189	0	0	Low
Rapid serologic testing	Screening of all or part of all blood donations	117,840	98	33,600	2,352	Low
Laboratory serological testing	Screening of all or part of all blood donations	212,520	96	129,900	412	Low

Estimates for intervention specific outcomes are calculated and provided

Note: For some outputs qualitative indications are required. For these the levels "Low", "Medium" or "High" may be assigned for each respective safety intervention.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	The technological requirements considering education of personnel and availability of materials and support. These affect the overall effectiveness of the intervention
No testing	Baseline situation where no testing is performed	162,000	189	0	0	Low
Rapid serologic testing	Screening of all or part of all blood donations	117,840	98	33,600	2,352	Low Medium High

Select the appropriate value from the pick list

3.2 Where applicable, enter a threshold value (the maximum value considered acceptable) for each outcome. These would refer, for instance, to the maximum acceptable expenditure or maximum number of fatalities. The numbers provided can be shown in the bar chart (see next section) if so required. Empty cells will be ignored in the bar chart.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity	Cost-effectiveness [US\$ per death prevented]
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	The technological requirements considering education of personnel and availability of materials and support. These affect the overall effectiveness of the intervention	Total net cost per additional number of deaths prevented. This provides an indication of the "value for money" of the intervention relative to the baseline situation
No testing	Baseline situation where no testing is performed	162,000	189	0	0	Low	-

Threshold value

250,000	100	100,000	1,500	Medium	150,000
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Enter the maximum value applicable or acceptable for each outcome. Consider the same units as defined on the input values sheet.

3.3 Provide a series of numbers indicating the order of importance for each of the respective outcomes considered relevant for this assessment. The lowest number indicates the most important outcome. The ranking provided will be used as the basis for the step-by-step assessment, where an increasing number of outcomes will be compared and discussed.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity	Cost-effectiveness [US\$ per death prevented]
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	The technological requirements considering education of personnel and availability of materials and support. These affect the overall effectiveness of the intervention	Total net cost per additional number of deaths prevented. This provides an indication of the "value for money" of the intervention relative to the baseline situation
No testing	Baseline situation where no testing is performed	162,000	189	0	0	Low	-

Order of importance of outcomes

5	1	2	3	4	6
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Enter the order of importance of the outcomes, starting with 1 for the most important outcome. Not all cells need to be filled out, however a sequence from one with an increment of one is required. Outcomes without a number assigned will be ignored in the step-by-step assessment.

3.4 A step-by-step assessment to determine the preferred strategy can be performed per user request. At the bottom of this worksheet a button is placed to initiate this assessment.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity	Cost-effectiveness [US\$ per death prevented]
<i>Option reference:</i>	<i>Description:</i>	Total cost of the safety intervention + cost of treatment of infected patients	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	The technological requirements considering education of personnel and availability of materials and support. These affect the overall effectiveness of the intervention	Total net cost per additional number of deaths prevented. This provides an indication of the "value for money" of the intervention relative to the baseline situation

Select type of outcome:

Threshold value

Order of importance of outcomes

250,000	100	100,000	1,500	Medium	150,000
5	1	2	3	4	6

Create step-by-step qualitative evaluation sheets

Press this button to initiate the step-by-step assessment.

Once the button is pressed, new tabs will appear on the worksheet for each step of the assessment: StepByStep2 contains the 2 most important outcomes only, StepByStep3 contains the 3 most important outcomes only, etcetera. Each of these comparator sheets will have a series of comment cells to record various considerations.

Quantitative estimates StepByStep2 StepByStep3 StepByStep4

Outcomes are listed in the order of importance as set by the user. It is up to the user to indicate the preferred option and reflect on and report the underpinning considerations, taking only the outcomes shown on the worksheet into account. Subsequently, the appropriateness of this selection is reviewed when one additional outcome is considered. This sequential assessment will allow for exploration and discussion of the relevance and interaction of various outcomes in a more holistic manner.

The table below shows the first analysis table of the Step-By-Step qualitative assessment. Please refer to the Case Study document for an extensive illustration of how to use these tables in an assessment.

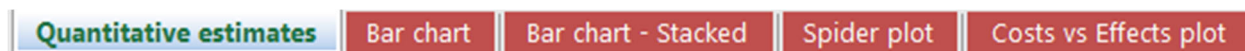
Optional Safety Interventions		Annual number of deaths [-]	Annual cost of the intervention [US\$]	Comments / Considerations
<i>Option reference:</i>	<i>Description:</i>	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	
No testing	Baseline situation where no testing is performed	189	0	
Rapid serologic testing	Screening of all or part of all blood donations	98	33,600	
Laboratory serological testing	Screening of all or part of all blood donations	96	129,900	
NAT testing	Screening of all or part of all blood donations	95	1,152,000	
Pathogen Reduction	Treatment of all or part of all blood donations with PR technology	104	600,000	

Cells for comments and considerations by the user

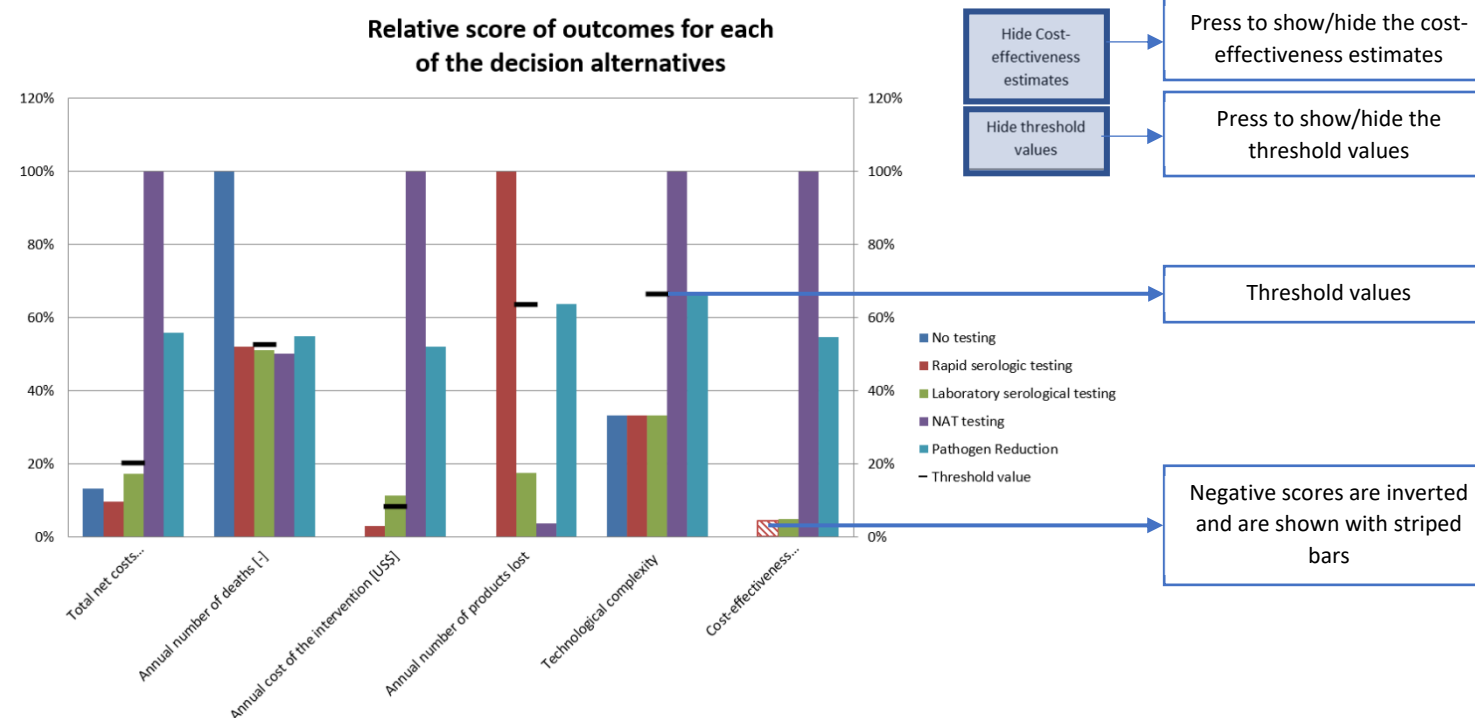
Outcomes assessed in the StepByStep2 tab

4. Generation of charts

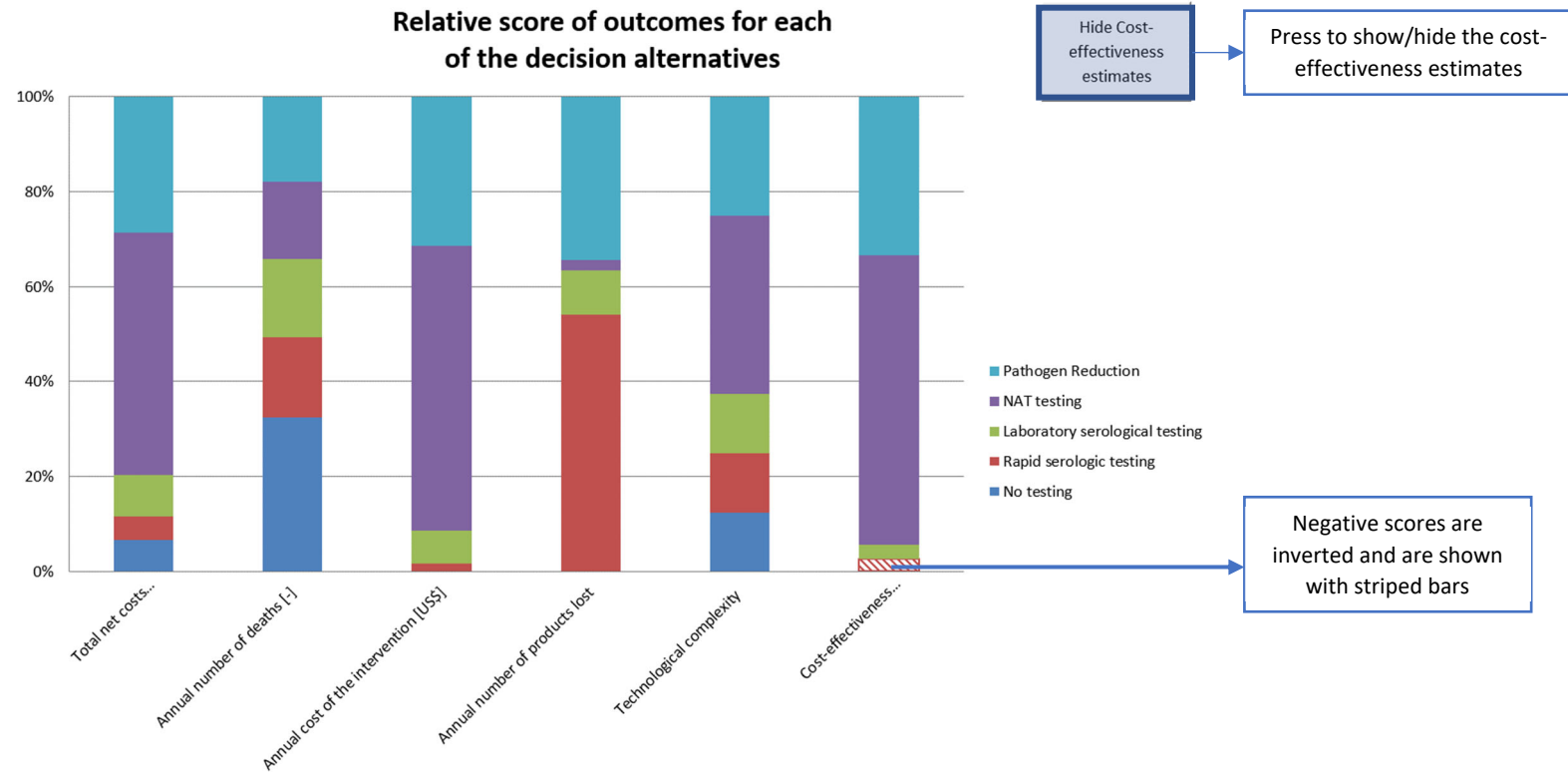
4.1 The data provided on the quantitative estimates sheet is used to produce different charts to aid in obtaining insight in the relative importance of each of the safety interventions. All values are scaled to the maximum value found over all interventions per outcome considered. Charts provided are bar charts (parallel and stacked), a spider plot and a cost-effectiveness plot. Despite the fact that the bar and spider plots visualize the same information, the user might have a preference for one of the presentation formats. Each chart can be found on a different tab from the workbook following the “Quantitative estimates” tab. The tabs for all charts have the same tab color.



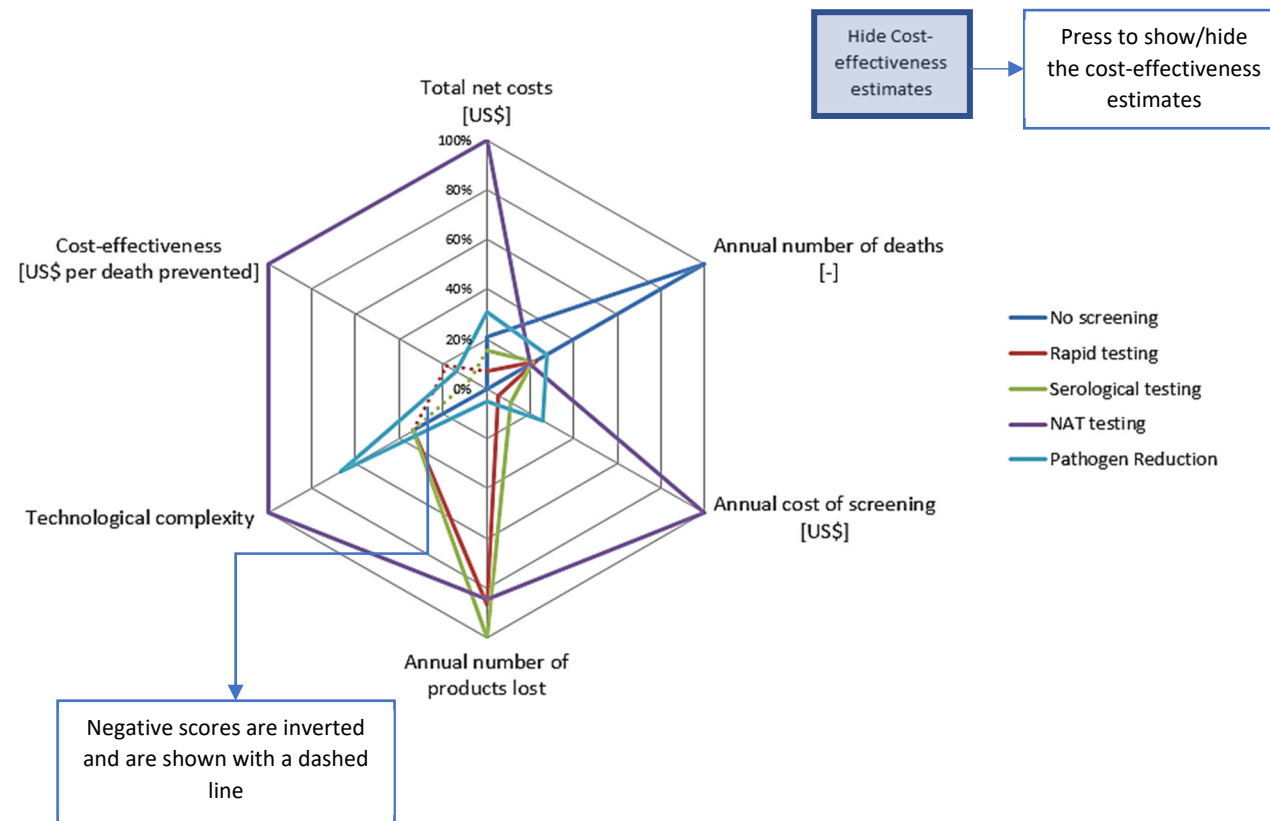
4.1.1 Bar chart: This chart type visualizes the relative score of each management option across all outcomes. The chart has two buttons. The first one allows the user to show/hide the cost-effectiveness estimates in the bar chart. The second one allows the user to hide/show the threshold values provided by the user (step 3.2).



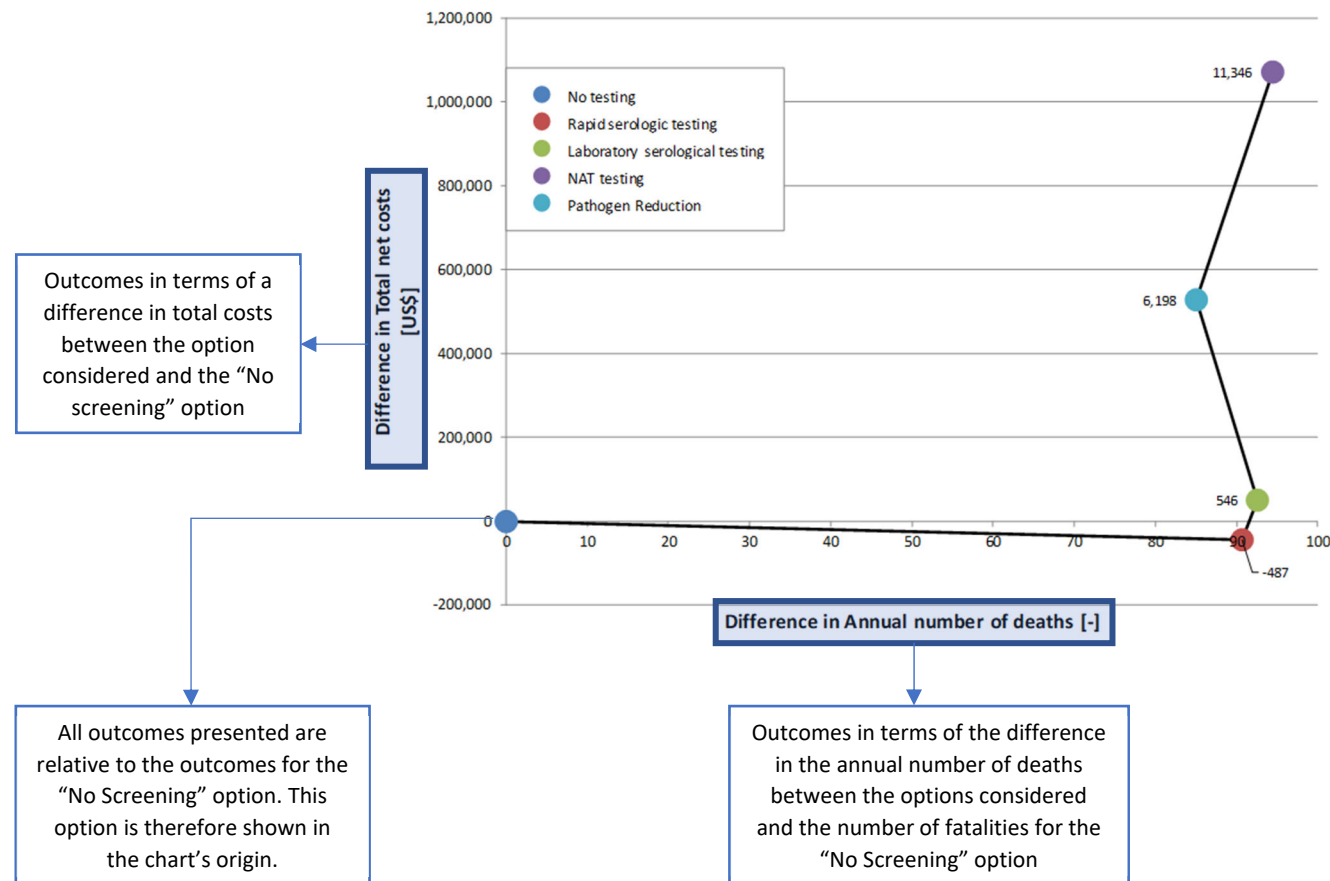
4.1.2 Bar chart - Stacked: This chart type again visualizes the relative score of each management option across all outcomes by setting the sum of all outcomes to 100%. The chart has only one button that allows the user to show/hide the cost-effectiveness estimates.



4.1.3 Spider-plot: This chart type again visualizes the relative score of each management option across all outcomes, but now in a two-dimensional plane. Like the previous chart, this chart has a button that allows the user to show/hide the cost-effectiveness estimates.



4.1.4 Cost-effects plot: This chart visually compares the different safety interventions outcomes in terms of differences in costs and fatalities. The chart shows the relative difference in costs and the annual number of deaths compared to the reference option (“No screening”). What can be found is that as a result of cases of transmission prevented, relative to “No screening” the total net cost for “Serological testing” and “Rapid testing” are less, whilst the annual number of deaths are substantially reduced as well.



5. MCDA assessment

5.1 The user can specify the weight for each of the outcomes in the bottom row of the assessment table. These weights will provide an equivalent value for the outcomes that should make them quantitatively comparable. The higher the MCDA equivalent value in the MCDA assessment table, the less favorable the outcome. Please refer to the User Guide or Case Study documentation for more information on how to assign these values.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [US\$]	Annual cost of the intervention [US\$]	Annual number of products lost [US\$]	Technological complexity [US\$]
<i>Option reference:</i>	<i>Description:</i>	Values provided (with the exception of the qualitative outcome) are the product of the column weight (bottom row) and the corresponding values provided on the 'Quantitative estimates' worksheet.				
NAT testing	Screening of all or part of all blood donations	1,233,081	13,999,986	0	13,054	300,000
Weights:		1	148,000	0	148	100,000
						300,000

Enter the appropriate weight for each of the outcomes

Note that there are two weights here: one for each level of increase in technological complexity

Description for the unit of the weighted outcomes: **US\$**

5.2 Enter the desired description for the common unit for the MCDA outcomes. This will be the unit for the weighted outcomes. In most cases this will be a monetary equivalent (so US\$ for instance).

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [US\$]	Annual cost of the intervention [US\$]	Annual number of products lost [US\$]	Technological complexity [US\$]
<i>Option reference:</i>	<i>Description:</i>	Values provided (with the exception of the qualitative outcome) are the product of the column weight (bottom row) and the corresponding values provided on the 'Quantitative estimates' worksheet.				
NAT testing	Screening of all or part of all blood donations	1,233,081	13,999,986	0	13,054	300,000
Weights:		1	148,000	0	148	100,000
						300,000

The description of the units for the weighted outcomes will be automatically copied to all column headers

Description for the unit of the weighted outcomes: **US\$**

Enter the desired indication for the units of the weighted outcomes

5.3 Once the weights and units are entered by the user, for each outcome of each safety intervention, the contribution to the MCDA total is calculated.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [US\$]	Annual cost of the intervention [US\$]	Annual number of products lost [US\$]	Technological complexity [US\$]
<i>Option reference:</i>	<i>Description:</i>	Values provided (with the exception of the qualitative outcome) are the product of the column weight (bottom row) and the corresponding values provided on the 'Quantitative estimates' worksheet.				
No testing	Baseline situation where no testing is performed	162,000	27,972,000	0	0	0
Rapid serologic testing	Screening of all or part of all blood donations	117,840	14,545,440	0	348,096	0
Laboratory serological testing	Screening of all or part of all blood donations	212,520	14,265,720	0	60,917	0
NAT testing	Screening of all or part of all blood donations	1,233,081	13,999,986	0	13,054	300,000
Pathogen Reduction	Treatment of all or part of all blood donations with PR technology	689,100	15,384,600	0	222,000	100,000
Weights:		1	148,000	0	148	100,000
						300,000

Weighted contributions for each of the outcomes per safety intervention which are determined by the weights shown

Note that a weight of 0 is applied for the annual costs of the intervention. This is because these costs are already accounted for in the total net costs.

5.4 On the worksheet, the total MCDA score is also shown, which is calculated by summation of the MCDA contributions per safety intervention. This is the product of quantitative estimates and outcome weights for quantitative outcomes and the sum of weights for each level of increase in technological complexity. The safety intervention with the lowest score is the "preferred option". Alternative or additional considerations may apply. These can be noted in the comments' cells per safety intervention.

Optional Safety Interventions		Annual cost of the intervention [US\$]	Annual number of products lost [US\$]	Technological complexity [US\$]	Overall MCDA score	Comments / Considerations
<i>Option reference:</i>	<i>Description:</i>	The exception of the qualitative outcome) are the product (bottom row) and the corresponding values provided on 'Quantitative estimates' worksheet.			Overall score is calculated as the sum of all weighted outcomes presented. These are the product of quantitative estimates and outcome weights	
No testing	Baseline situation where no testing is performed	0	0	0	28,134,000	
Rapid serologic testing	Screening of all or part of all blood donations	0	348,096	0	15,011,376	
Laboratory serological testing	Screening of all or part of all blood donations	0	60,917	0	14,539,157	
NAT testing	Screening of all or part of all blood donations	0	13,054	300,000	15,546,121	
Pathogen Reduction	Treatment of all or part of all blood donations with PR	0	222,000	100,000	16,395,700	
Weights:		0	148	100,000 300,000		

Overall MCDA scores calculated by the tool

Space to enter additional comments and/or considerations by the user

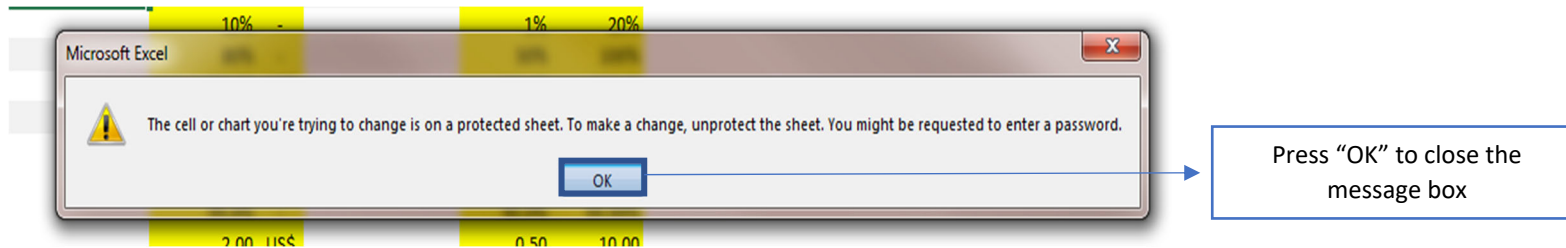
6. MCDA
Sensitivity
Assessment

6.1 In addition to the assessment, the multiple criteria decision making (MCDM) support tool also provides the values corresponding to “changepoints” in the model parameters, where a change in the preferred safety interventions will occur. E.g. for the parameter “Sensitivity of Rapid serologic testing”, within the range 65% to 99.99% a change of the preferred safety intervention from 3 (“Laboratory serological testing”) to 2 (“Rapid serologic testing”) is found at a sensitivity of 94.4% for this test.

Current preferred option: Laboratory serological testing						Current preferred option found by the MCDM assessment
Model parameter description	Value	Units	Min Value	Max Value	Changepoints	
Number of donations	60,000	-	60,000	60,000		
Prevalence among donors	2%	-	1%	20%	At 10% a change from 3 to 4;	
Proportion recipients not affected	10%	-	1%	20%		
Coverage rate for the safety intervention	50%	-	50%	100%		Description and point estimate for the model parameter
Costs of treatment (per patient)	150.00	US\$	100.00	200.00		
Mortality rate of infected patients	17.5%	-	10%	20%		
Sensitivity of Rapid serologic testing	96.0%	-	65%	99.99%	At 99,4% a change from 3 to 2;	Minimum and maximum values considered for the MCDA sensitivity assessment
Specificity of Rapid serologic testing	92.0%	-	80.0%	99.99%		
Costs of Rapid serologic testing (per donation)	1.12	US\$	0.50	2.50		
Sensitivity of Laboratory serological testing	98.0%	-	75%	99.99%	At 94,6% a change from 2 to 3;	At 94,4% the best option changes from Option 3 (Laboratory serological testing) to Option 2 (Rapid serologic testing)
Specificity of Laboratory serological testing	98.6%	-	98.0%	99.99%		
Costs of Laboratory serological testing (per don.)	4.33	US\$	3.25	5.40		
Sensitivity of NAT testing	99.9%	-	99.4%	99.99%		
Specificity of NAT testing	99.7%	-	99.6%	99.80%		
Costs of NAT testing (per donation)	38.40	US\$	24.90	59.50		
Effectivity of Pathogen Reduction	90.0%	-	75%	99.99%		
Costs of Pathogen Reduction (per donation)	20.00	US\$	15.00	30.00		
Production loss of Pathogen Reduction	5.0%	-	3%	7%		
MCDA weights for						
Total net costs	1.00	-	1	1		
Annual number of deaths	148,000	US\$/death	0	1,500,000	At 1.203 a change from 1 to 3; At 708.830 a change from 3 to 4;	
Annual cost of the intervention	0	-	0	0		
Annual number of products lost	148	US\$/product	0	5,000	At 3.262 a change from 3 to 4;	
Medium Technological complexity	100,000	US\$	0	1,500,000		
High Technological complexity	300,000	US\$	0	1,500,000		
Risk management options considered:						
1: No testing						
2: Rapid serologic testing						
3: Laboratory serological testing						
4: NAT testing						
5: Pathogen Reduction						
List of optional safety interventions. The numbering refers to the indication of the preferred options at the changepoints indicated						

General considerations:

- The user can increase or decrease the height of a selected row of a table by pressing the keys <Ctrl> + <H> or <Ctrl> + <L> respectively (Higher/Lower). To increase or decrease the width of the selected column in a table press <Ctrl> + or <Ctrl> + <N> respectively (Broader/Narrower). Using these commands will ensure that the overall layout of the associated tables remains identical.
- All non-input cells in the workbook are protected to prevent incidental changes. The following message will appear if the user tries to change a protected cell.



To override this protection, press "Unprotect Sheet" under the review tab in the excel menu. There is **no password required** to change the worksheet protection mode. This allows an experienced user to change for example any of the calculations made if so desired.

