THE
VALUE OF INFORMATION FOR CARDIOVASCULAR TRIALS AND OTHER COMPARATIVE RESEARCH (VICTOR) PLATFORM

User Guide

April 2, 2018

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A. OVERVIEW

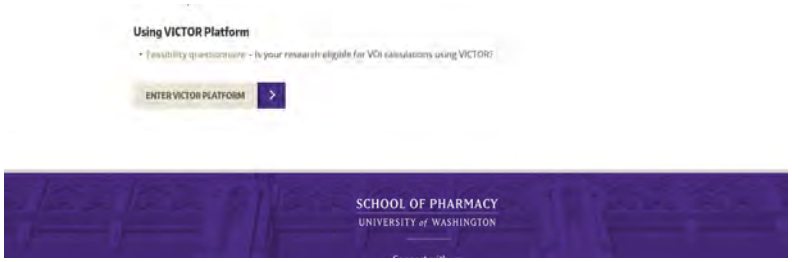
This section reviews the steps to be followed to carry out value of information calculations using the VICTOR platform (https://sop.washington.edu/choice/research/research-projects/victor/). The steps are:

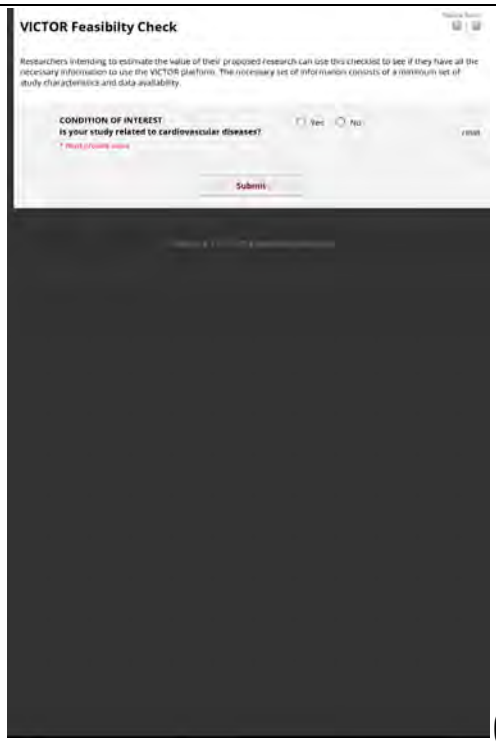
1. Feasibility Check
2. Enter VICTOR Platform - Orientation
3. Enter Study Parameter Values
4. Enter Clinical Parameter Values

We now discuss each step below.

A 1: FEASIBILITY CHECK

To check the feasibility of a research study for VICTOR, one should click on the "Feasibility Questionnaire" on the VICTOR Page. This will bring the user to a REDCAP-based survey page (Figure 1a) and ask the user to answer a series of questions. If the user is able to answer "YES" to all the questions, then the research study should be feasible for valuing using the VICTOR Platform (Figure 1b).





(a)

(b)

Figure 1: (a) VICTOR Feasibility Check Questionnaire; (b) Answering "YES" to all questions indicates feasibility for using VICTOR to value research proposal.

A 2: ENTER VICTOR PLATFORM AND ORIENTATION

Once you click on the "ENTER VICTOR PLATORM", it will bring you to the main VICTOR page. There are 9 parts of this page that are worth orienting yourself before starting to enter data. Parts 1- 6 are illustrated in Figure 2. Parts 7 – 9 are illustrated in Figure 3.

Figure 2 : Orient to VICTOR Platform Parts 1 - 6

1. Page for Study Parameters Input
2. Expression of Intervention Effects and Endpoints on the Study Parameters Page.
3. Page for Clinical Parameters Input
4. Run EVPI
5. Results for EVPI
6. Hide Parameters Page and Enlarge Results Section

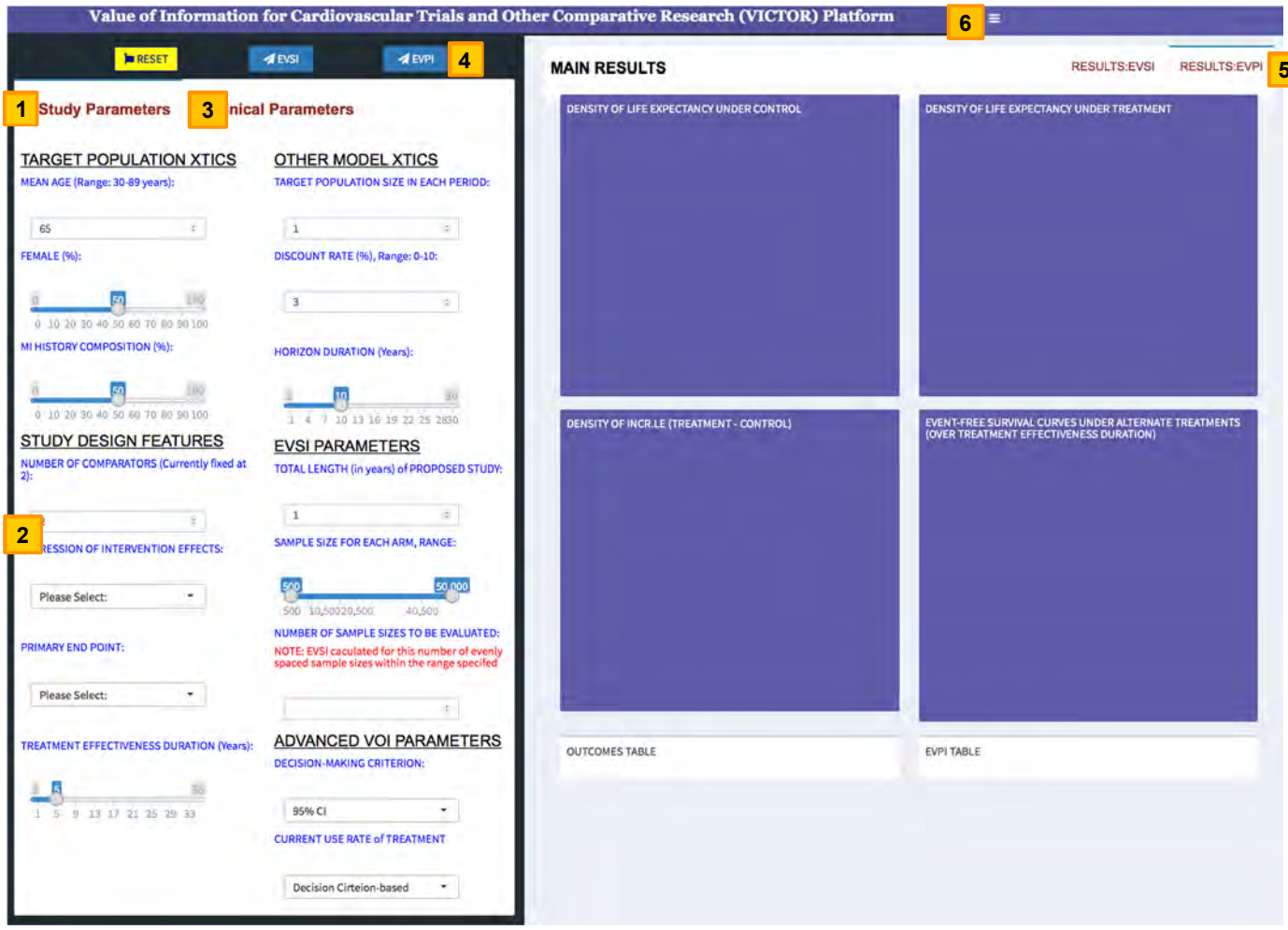
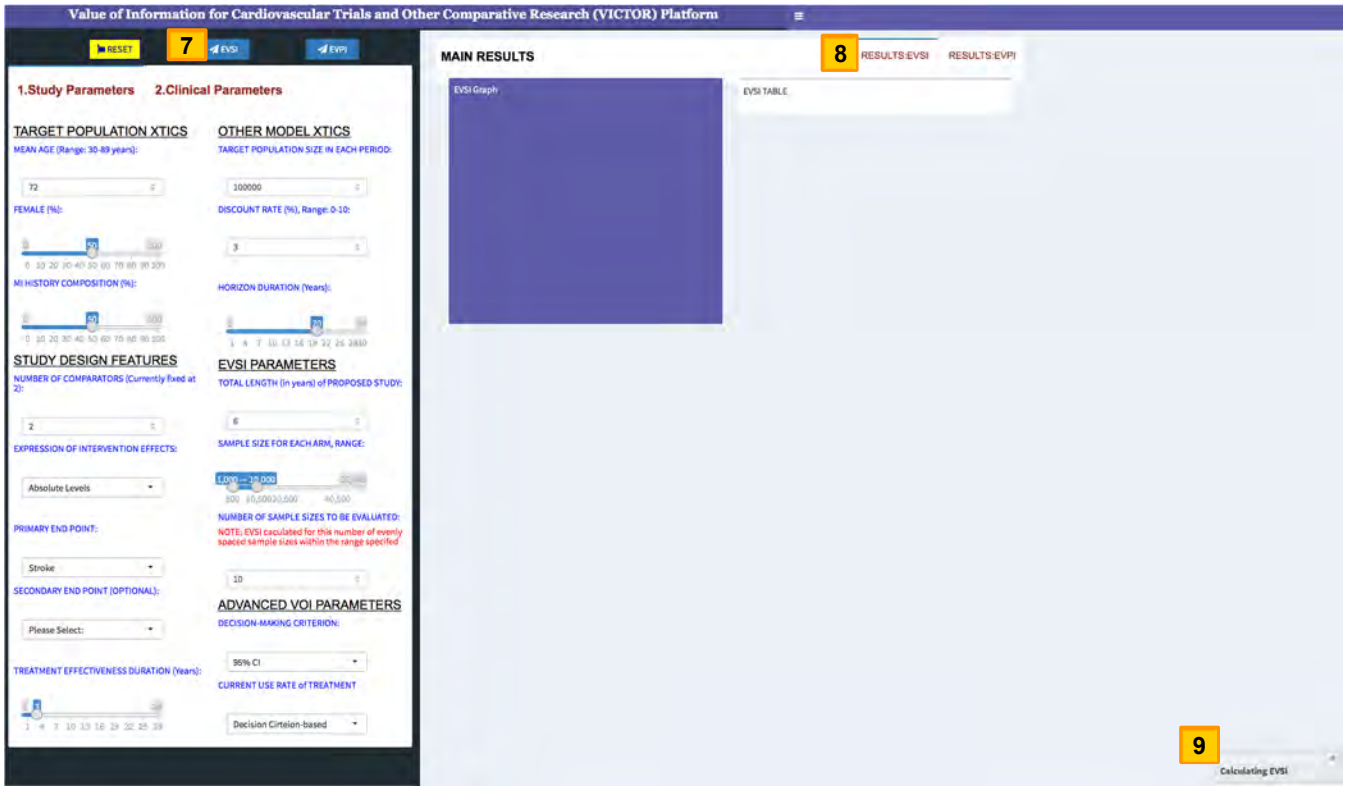


Figure 3: Orient to VICTOR Platform Parts 7-9.

1. Run EVSI
2. Results for EVSI
3. Showing Process of EVSI Calculation (only appear when EVSI calculation starts)



A 3: ENTER STUDY PARAMETER VALUES

This section seeks a list of parameter values related to the study population and design needed for VOI calculations. The default value of each indicates that value that will be used by the VICTOR model if no user input is provided. Where no default value is provided, it indicates that user input is mandatory.

1. Study parameters

- TARGET POPULATION XTICS
    - **Mean Age** – mean age of the study population (Range: 30 – 89 years, Default: 65 years)
    - **Female (%)** - % females in the study (Default: 50%)
    - **MI history composition** - % with MI history (Default: 50%)
- STUDY DESIGN FEATURES
    - **Number of comparators**
        - Fixed at 2 (currently only allows to calculate VOI for two-arm studies, e.g. treatment versus control)
    - **Expression of intervention effects** - this indicates the scale in which treatment effects will be expressed)
        - Absolute level
        - Risk different
        - Ln(HR), Ln(RR)
    - **Primary endpoint** – Choose primary end-point for the study
        - All-cause mortality
        - Stroke
        - MI
        - MACE
    - **Secondary endpoint** – Choose secondary end-point for the study
        - Bleeding
        - Stroke
        - MI
    - **Treatment effectiveness duration (years)** - number of years over which treatment effect persists in a typical patients (Default: 5 years)

- OTHER MODEL XTICS
    - **Target population size in each period** - number of patients every year affected by the comparative decision that the proposed study seeks to inform (Default: 1)
    - **Discount rate** – rate at which future life-years will be discounted (Default: 3%)
    - **Horizon duration (years)** - number of years that the comparative decision that the study seeks to inform will be relevant for clinical decision-making. (Default: 10 years)
- EVSI PARAMETERS – these parameters only come into play when VOI is to be conducted for study(ies) of specific sample sizes
    - **Total length of proposed study** – duration from start to end of the proposed study (in years, Default: 1 year)
    - **Sample size for each arm** – this asks for a range of sample sizes for each arm of the study – assumes a 1:1 allocation, Default: 500 – 50,000)
    - **Number of sample size to be evaluated** – this ask for the number of specific sample sizes to be evaluated within the range specified in the previous question. EVSI is calculated for this number of evenly spaced sample sizes (per arm) within the range specified). For example, if range specific is 500 – 10,500 and this number specified is 3, EVSI will be calculated for three different studies, one with 500 patients per arm, another with 5500 patients per arm, while a third with 10,500 patients per arm.
- ADVANCED VOI PARAMETERS
    - **Decision-making criterion** – evidence criterion for adoption/rejection of treatment
        - 95% CI (Default)
        - Expected value
    - **Current use rate of treatment** – can specify if current use of treatment defies any of the evidence criterion suggested. If this is selected, VICTOR will ask what fraction of the population uses treatment currently.

A 4: ENTER CLINICAL PARAMETER VALUES

This section seeks a list of annual event rates for the control and treatment arm of the proposed study. The control arm rates must be provided in annual absolute rates. The treatment arm rates can be provided based on the scale of intervention effect selected in the "Study Design Features" in the previous section.

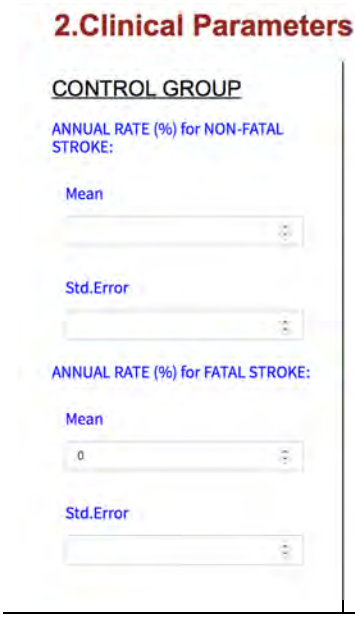
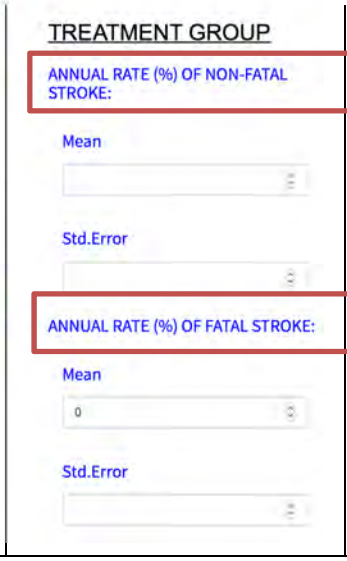
The events for which rates will be sought will depend on the chosen primary and secondary endpoints in the previous section.

Illustrated below is the list of clinical parameters needed, when the primary end-point is chosen to be "STROKE" and no secondary end-point is chosen.

2. Clinical parameters

Options for Clinical Parameters

- depend on the Expression of Intervention Effects and Endpoints

	Expression of Intervention effects (chosen under Study Design Features)		
	Absolute level Annual rate (%)	Risk different Annual incremental rate(%)	Ln(HR), Ln(RR) Ln(HR)/ Ln(OR) / Ln(RR) of treatment
			

B. AN EMPIRICAL EXAMPLE

B 1. THE VALUE OF INFORMATION FOR THE SHEP STUDY

The Systolic Hypertension in the Elderly Program (SHEP) was a randomized double-blinded clinical trial to evaluate the efficacy of intervention for hypertension using placebo as the control group. SHEP recruited patients who aged 60 and older with isolated systolic hypertension (ISH) from 1985 to 1988, and followed them up for 5 years. The primary endpoint was fatal and non-fatal stroke. The result of SHEP pilot Study was published in 1988, showing average age of 551 participants was 72 years old, 63% was female, and average follow up time was 34 months. We seek to estimate the expected value of this proposed study, without taking into account any of the results from the actual study. All calculations are based on information available in the original protocol for the study.

B 2. APPLYING FEASIBILITY CHECKLIST

- Required information: minimum set of study characteristics and data availability

FEASIBILITY FACTOR	FEASIBILITY QUESTION	FEASIBILITY CHOICE SET EXAMPLE - SHEP	
STUDY POPULATION:	Is the condition of interest for your study population listed?	Patients with hypertension	**Y/N**
STUDY TYPE:	Is your proposed study design listed?	2 arm (anti-hypertensive treatment vs. placebo)	**Y/N**
ENDPOINTS:	Is your proposed primary study endpoint listed?	Fatal and non-fatal stroke	**Y/N**
INTERVENTION EFFECTS:	Can the effect of the intervention in your proposal be expressed using one of the options listed?	Annual rates (%) for fatal and non-fatal stroke are available for both groups	**Y/N**
BACKGROUND CLINICAL DATA FOR CONTROL GROUP, BY ENDPOINT	Do you have listed data on the control group for the primary endpoint?	Annual rate (%) for both fatal and non-fatal stroke, mean (se)	**Y/N**
BACKGROUND CLINICAL DATA ON INTERVENTION EFFECTS, BY ENDPOINT	Do you have listed data on selected intervention effects?	Annual rate (%) for both fatal and non-fatal stroke for intervention group, mean (se)	**Y/N**

B 3. STUDY PARAMETERS INPUT FOR SHEP PROTOCOL

Study Parameters

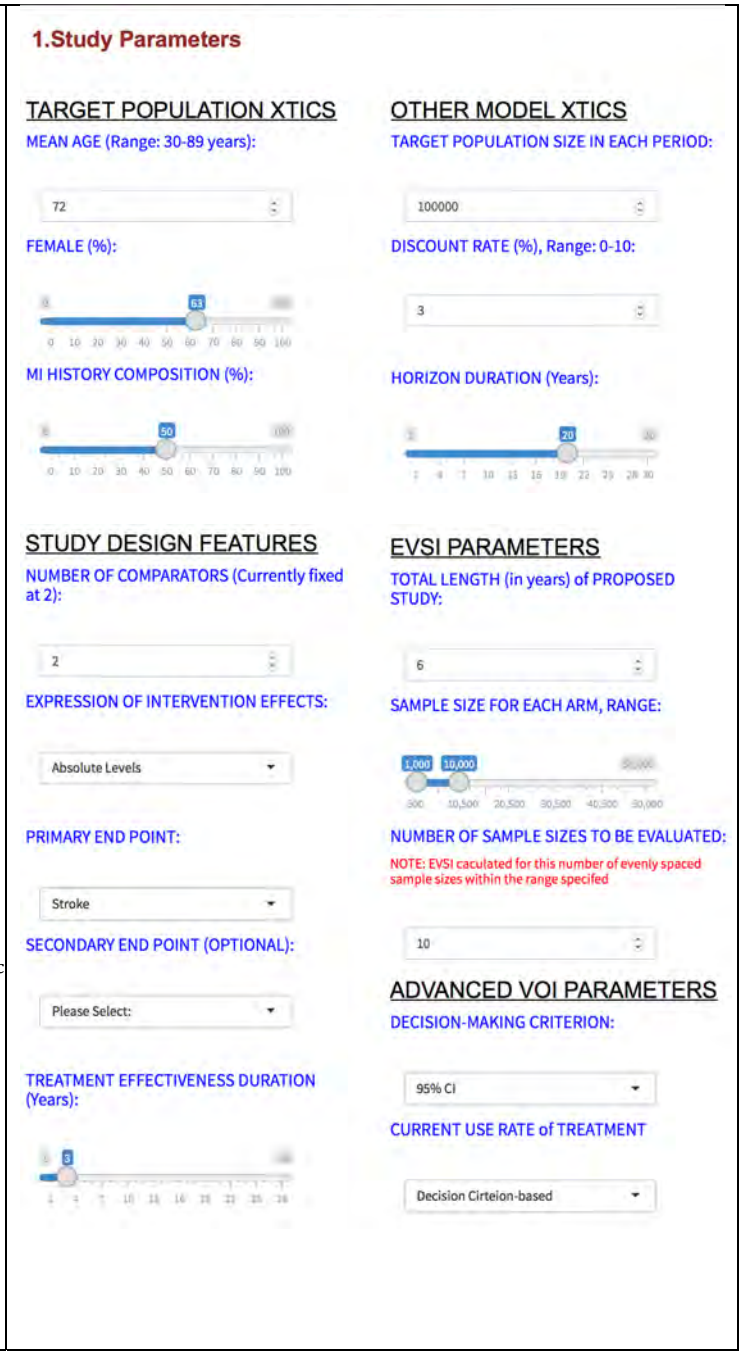
- **Target population**
  - Mean Age : 72
  - Female(%) : 63
  - MI history composition (%) : 50

- **Study design features**
  - Number of comparators (Fixed at 2)
  - Expression of intervention effects : Absolute level
  - Primary endpoint : Stroke (included fatal & non-fatal stroke)
  - Treatment effectiveness duration : 3

- **Other model input**
  - Target population size : 100,000 [a]
  - Discount rate(%) : 3
  - Horizon duration (years) : 20

- **EVSI parameters**
  - Total length of proposed study : 6 [b]
  - Sample size for each arm : 1,000-10,000 [c]
  - Number of sample size to be evaluated : 10 [c]

- **Advanced VOI parameters**
  - Decision-making criterion : 95% CI
  - Current use rate of treatment : Decision-making criterion



NOTE:

[a] some outcomes would be 0 if target population size is too small because the outcomes are presented in "millions years".

[b] according to the SHEP pilot study, mean follow up time was 34 months and enrollment of the SHEP trial was from 1985-1988

[c] (10000- 1000)/(10-1)=1000 → VICTOR will show the results of EVSI for every 1,000 sample size for each arm from 1,000 to 10,000

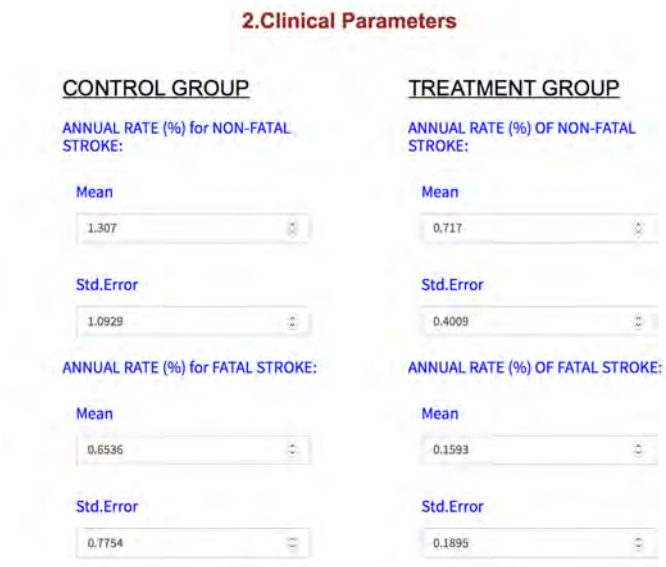
B 4. STUDY PARAMETERS INPUT FOR SHEP PROTOCOL

Control group

a. annual rate (%) for non-fatal stroke : 1.307 ± 1.0929
b. annual rate (%) for fatal stroke : 0.6536 ± 0.7754

Intervention group

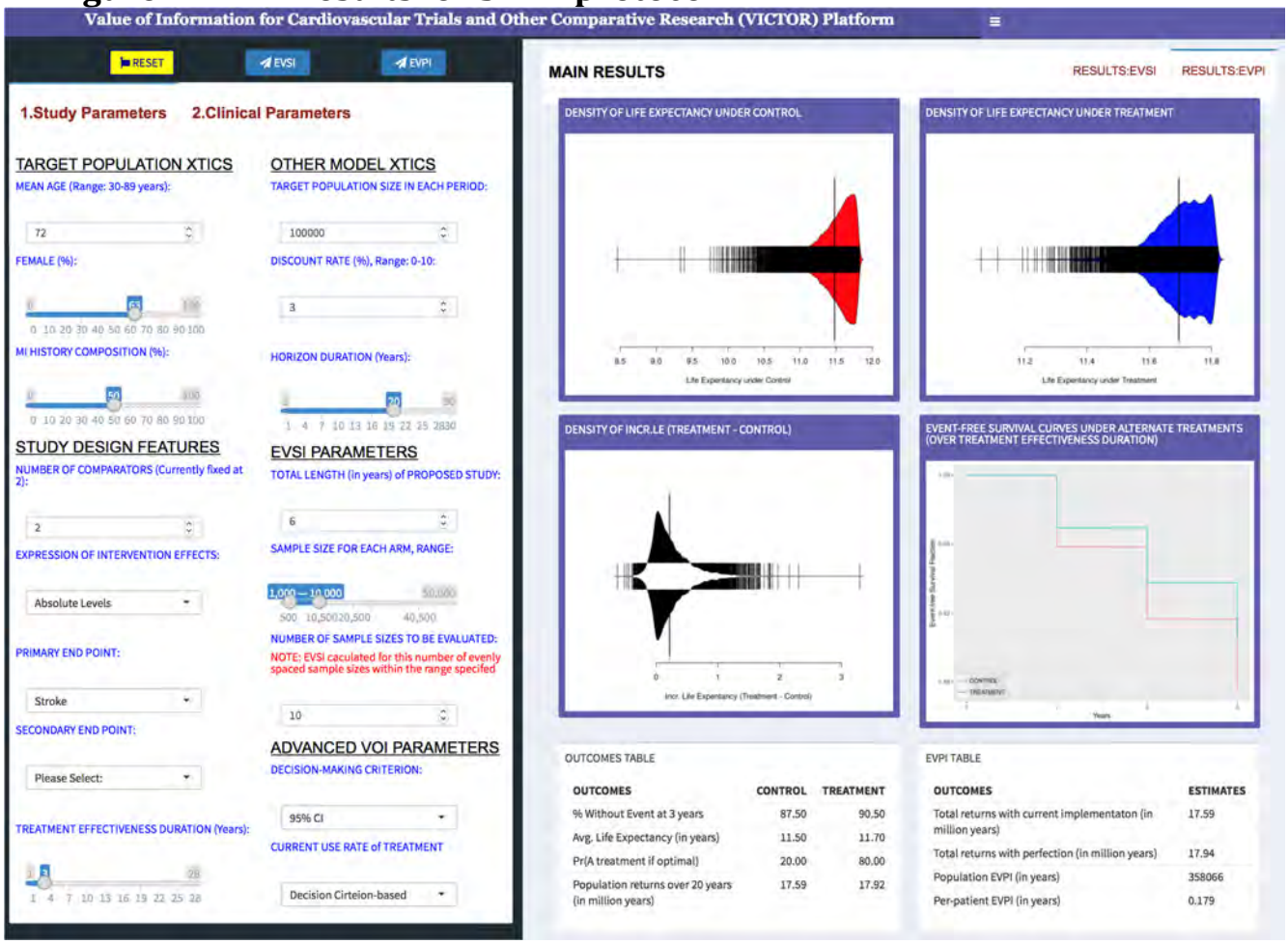
a. annual rate (%) for non-fatal stroke : 0.717 ± 0.4009
b. annual rate (%) for fatal stroke : 0.1593 ± 0.1895



B 5. RUN EVPI ON SHEP PROTOCOL

- The top 2 figures are density of life expectancy for control and intervention group; the middle 2 figures are density of incremental life expectancy and event-free survival curve (Green line for intervention group and red line for control group)
- The bottom left table shows the outcomes for intervention and control group, including the percentage of patients without any event at 3 years, average life expectancy in years, probability of the treatment if it is optimal, and population returns over 20 years in million years.
- The bottom right table shows the estimates of EVPI calculation, including total returns with current information and perfect information that both are reported in the millions years, and population and per patient EVPI in years.

Figure 4: EVPI Results for SHEP protocol



B 6. RUN EVSI ON SHEP PROTOCOL

- In the EVSI graph, X-axes represents sample size per arm, and Y-axes shows population EVSI in years. The EVSI table shows population EVSI as well as per patient EVSI in years for different sample size per arm.
- In our example, we report the EVSI calculation for every 1,000 sample size per arm from 1,000 to 10,000.

Figure 5: EVSI results for SHEP Protocol.