

## Test case of the CORE-MD risk calculator, October/November

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Several adjustments to the risk calculator have been made. A new version has just been uploaded to [https://jwavanegeraat.shinyapps.io/COREMD\\_RiskCalculatorV4/](https://jwavanegeraat.shinyapps.io/COREMD_RiskCalculatorV4/). Changelog:

- It can now generate graphs comparing 2 devices.
- I've simplified the label for the y-axis. In my opinion "Smallest 1-year risk that can be excluded with 95% probability" is too difficult to grasp. I oversimplified it to "risk", why including extra information in the caption of the graph.
- On request by Alan Fraser, it also generates graphs which would be more useful to patients.

Please give it a try.

### Purpose of the Calculator

The calculator generates 2 types of graphs.

The calculator first takes as input the amount of events and the amount of patient years from a particular study. From this, it computes an event rate.

Given that event rate, the calculator answers the question:

- If we did a study with x amount of patient years, and we'd find the same event rate as computed before, what does this tell us about the n-year risk for an individual device? The graph answers with an upper bound to the n-year risk, for a certain confidence level p.
- x, n and p are all tweakable parameters.

For the second graph, the calculator generates a graph meant for an individual patient deciding whether to get a device. It shows an upper bound to the n-year risk, based on the observed study results. See the results in the next section for some examples.

\*\*\* all is based on the assumption of constant hazard \*\*\*

## Test case

I've used results from the ABSORB II trial, supplied by Georgios Siontis. In this trial, the "failed" BVS device was compared to the EES device. The data is summarised in the following table. The study took 4 years. At the end of each year, the results were published. As can be seen, the EES had less adverse events throughout the entire study duration. The question is whether the study should have stopped earlier, given the worse performance of BVS. The CORE MD risk calculator aims to provide an answer.

Year	Observed cumulative number of events		Observed cumulative device experience		Observed Rate		Upper limit to 5 year risk	
	BVS	EES	BVS	EES	BVS	EES	BVS	EES
1	3	0	335	166	0,008955	0	0.11	0.09
2	5	0	660	329	0,007576	0	0.07	0.04
3	9	0	980	488	0,009184	0	0.08	0.03
4	9	0	1269	627	0,007092	0	0.06	0.02

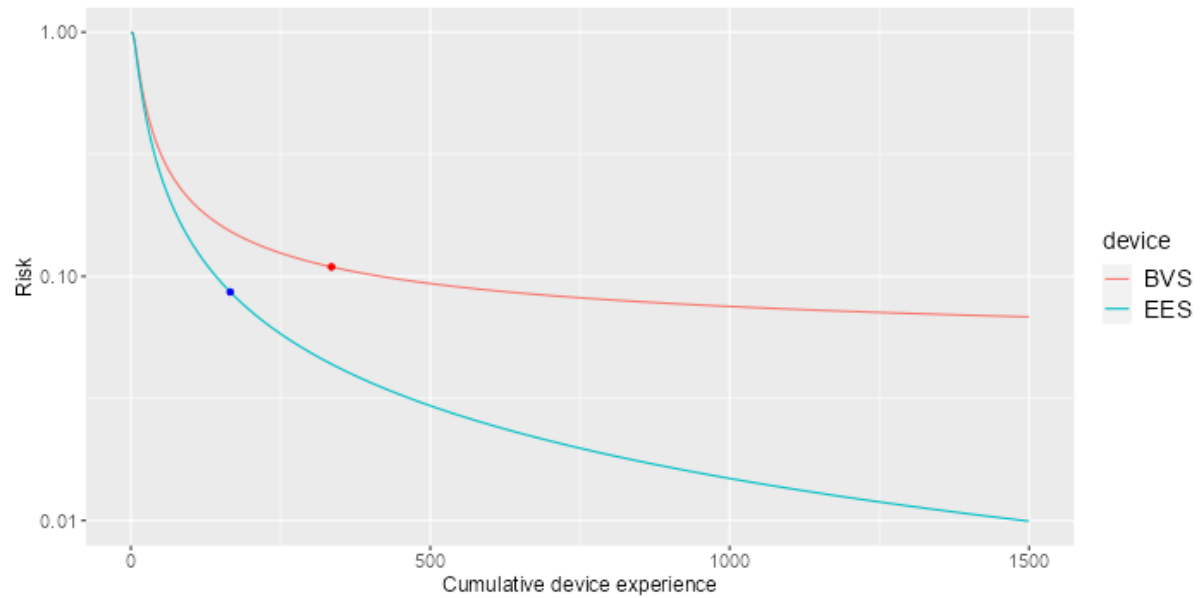
The numbers going in to the calculator are given in the columns <observed number of events> and <observed cumulative device experience>. The last column (upper limit to 5 year risk) can be read of from the graph. The upper limit decreases as confidence increases. We are 95% sure the 5 year risk is below the given number.

In the next part, I will generate 4x2 graphs: one graph for regulators and one graph for patients for each year of the study.

The graph for regulators will show the upper limit to the 5-year risk of the device. The upper limit is given with 95% confidence, but the confidence level can be changed.

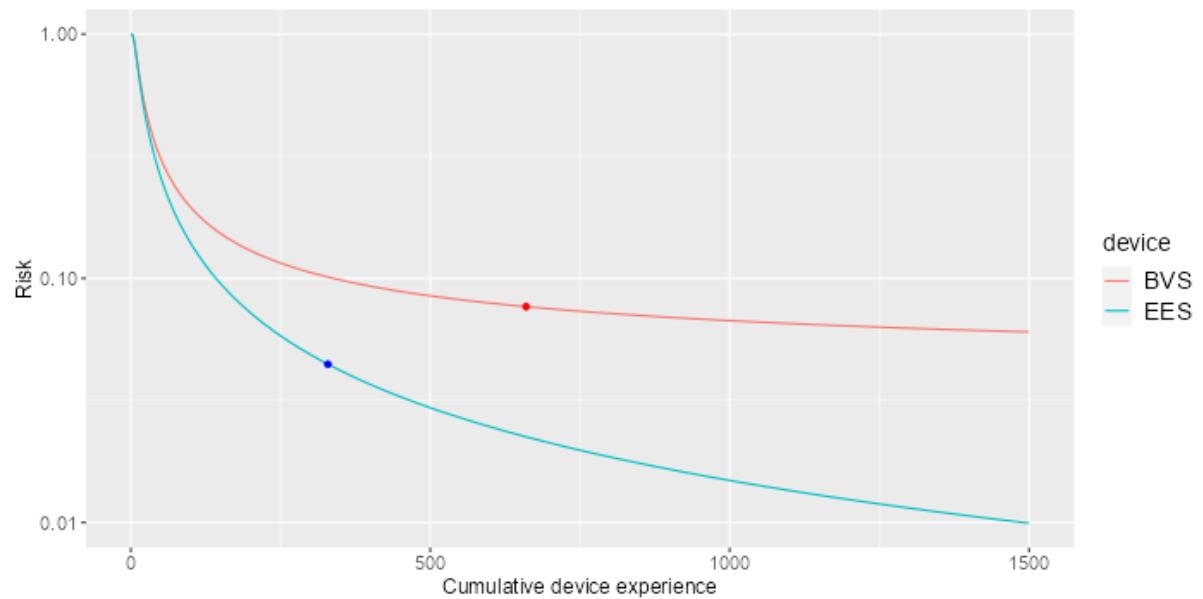
## "Regulator" graphs

Risk as function of total cumulative device experience, based on year 1

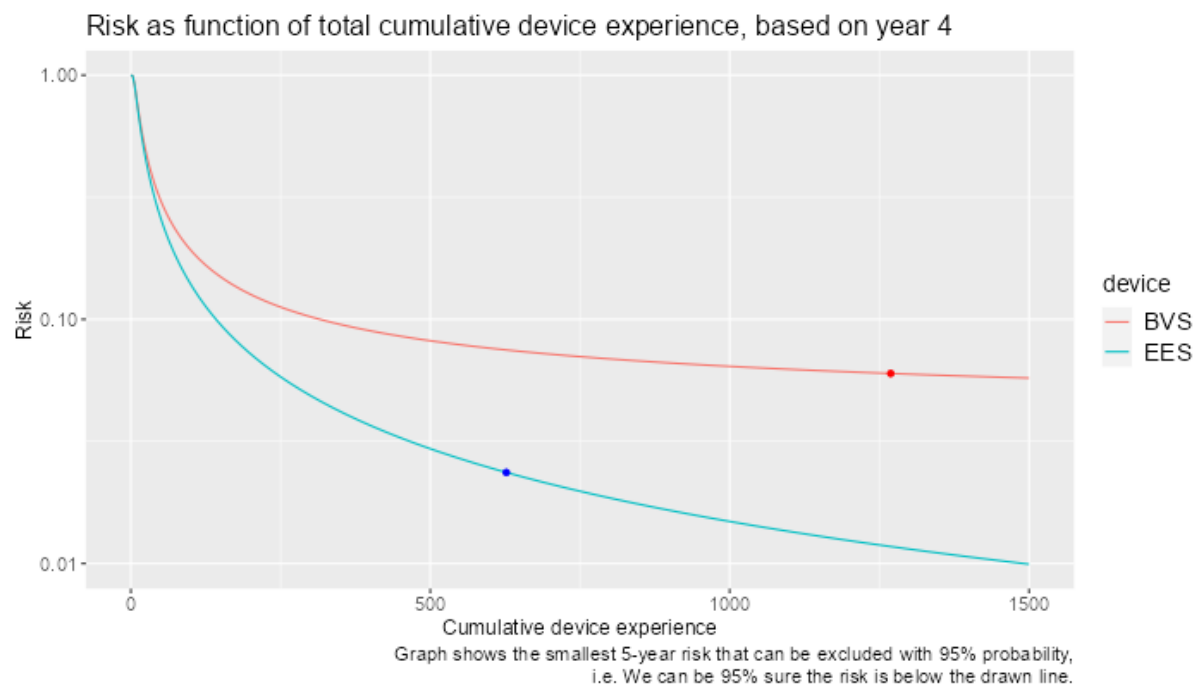
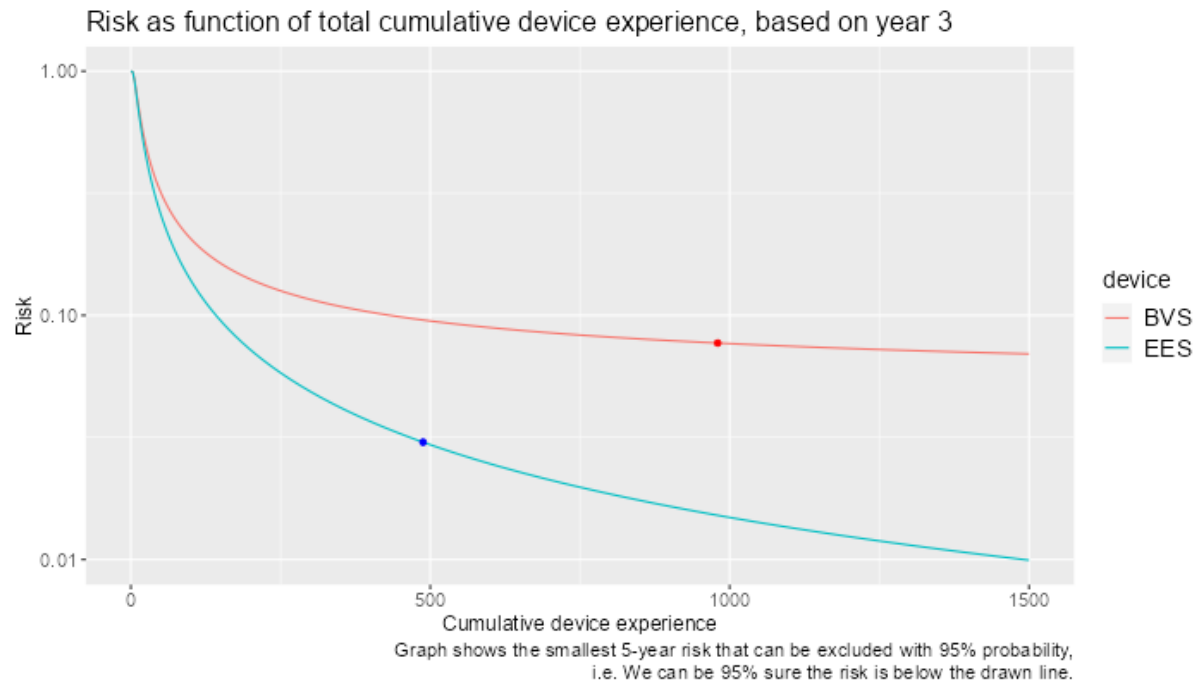


Graph shows the smallest 5-year risk that can be excluded with 95% probability, i.e. We can be 95% sure the risk is below the drawn line.

Risk as function of total cumulative device experience, based on year 2



Graph shows the smallest 5-year risk that can be excluded with 95% probability, i.e. We can be 95% sure the risk is below the drawn line.



The dots mark the upper bound to the n-year risk that we computed for the observed event rate and the observed cumulative device experience, for which we are 95% sure. The rest of the graph is a sort of extrapolation: “had we done a study with less/more cumulative device experience, with the same event rate, this is the upper bound for the risk”. Because we compute a new event rate for each year, I give 4 graphs.

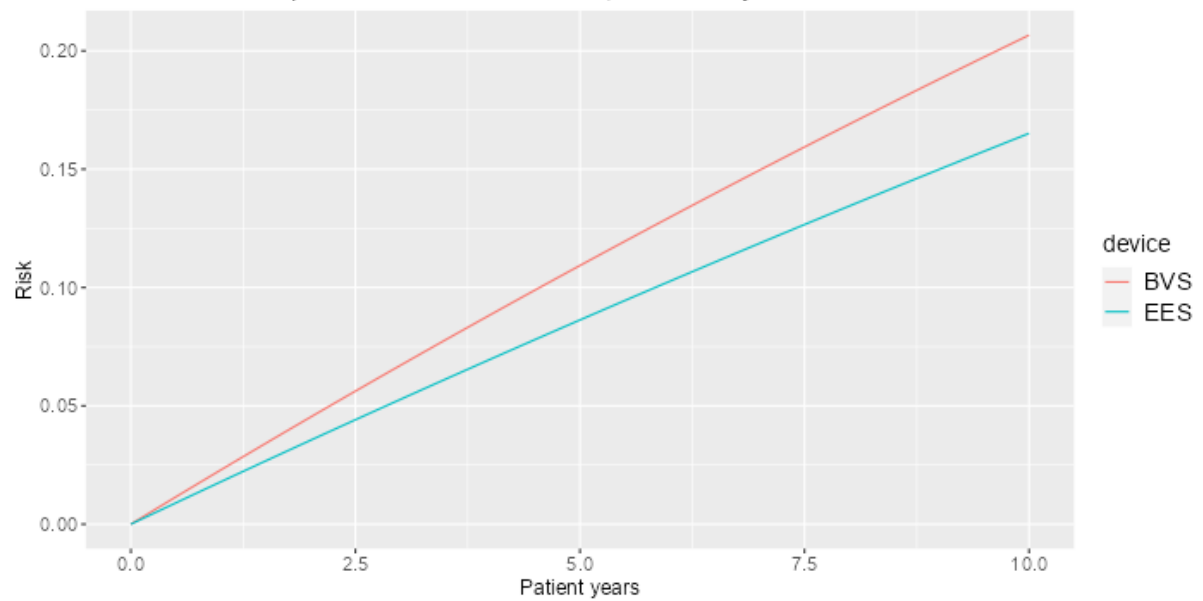
In all graphs it can be seen that EES is the superior device. Based on the first graph, we see that the 5-year risk for a BVS device is slightly higher than 0.10, while for EES it is slightly lower than 0.10. The important thing to realise is that by collecting more evidence, i.e. exposing more patients to this device, the upper bound to the BVS risk can be reduced to ~0.08, while by collecting more evidence for EES, we can reduce the upper bound to the risk 0.01. **Note we are not actually lowering the risk,**

**we only become more confident about the risk.** Thus, based on the results of the first graph, we can already ask ourselves if we need to expose more patients to the new device.

The computations are repeated for the results at the end of year 2, 3 and 4. All graphs confirm the expected results that can be read of the first graph.

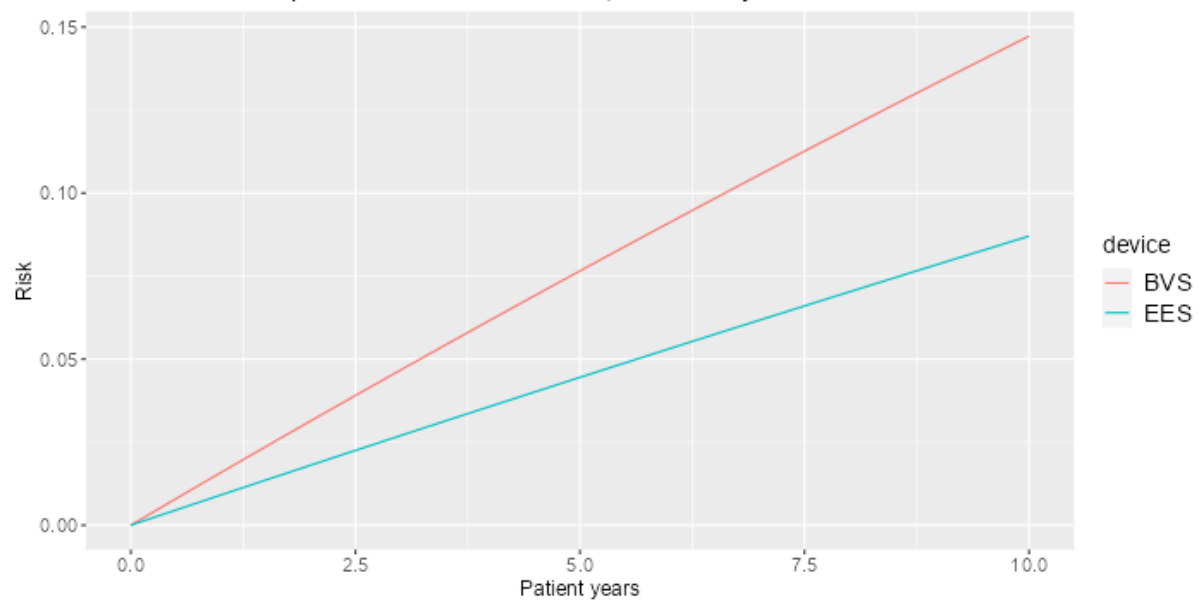
## "Patient" graphs

Device risk for a patient as function of time, based on year 1

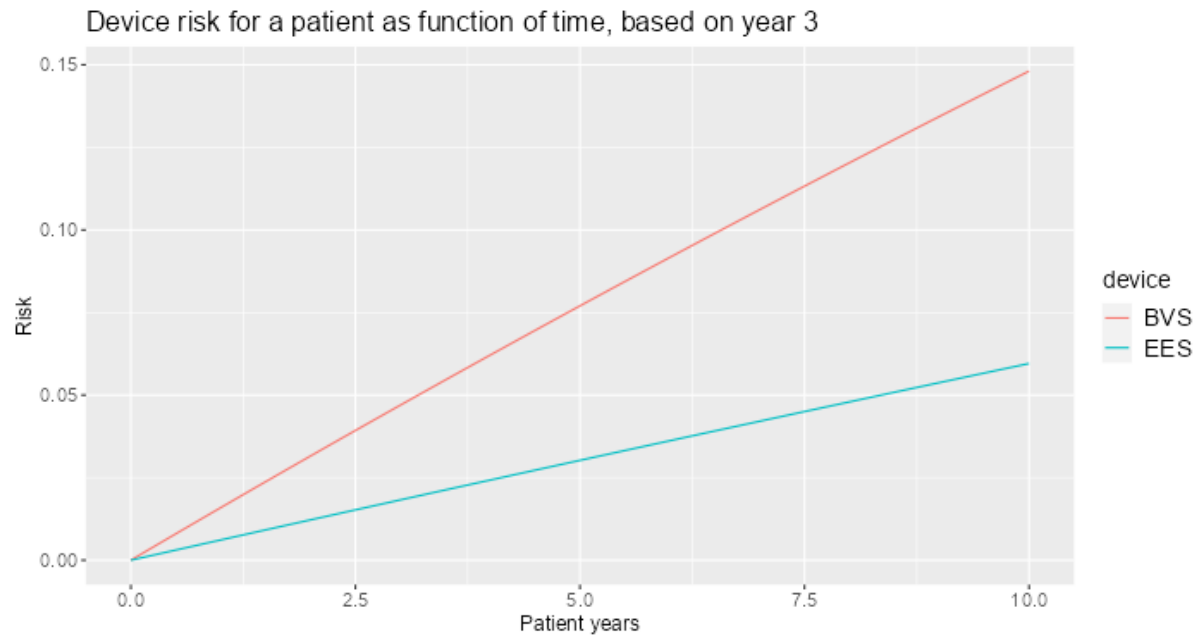


Graph shows the smallest risk that can be excluded with 95% probability,  
i.e. We can be 95% sure the risk is below the drawn line.

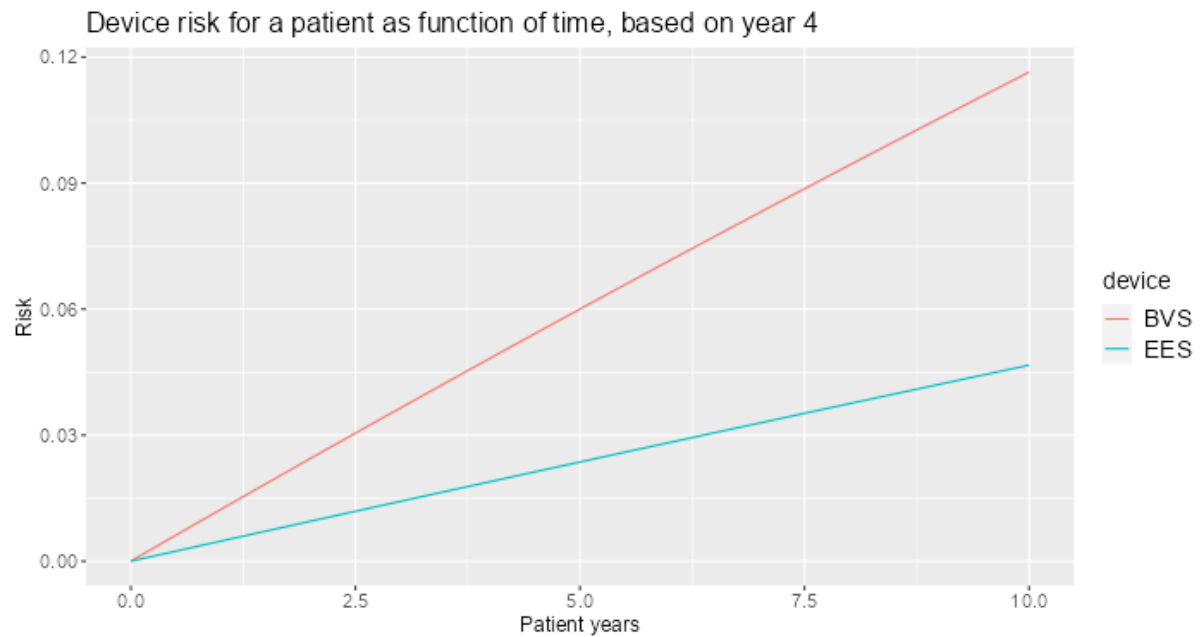
Device risk for a patient as function of time, based on year 2



Graph shows the smallest risk that can be excluded with 95% probability,  
i.e. We can be 95% sure the risk is below the drawn line.



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All graphs show again EES is superior device. The difference between the risks gets bigger as more evidence is collected. This is due to the increase in confidence. The event rate for EES was 0 at all time points, but 0 events in 627 patient years says more than 0 events in 166 patient years. The event rate of BVS does fluctuate a bit, but is higher than EES' event rate at all time points.