PROJECT: FLEXIBLE PROGRAM OPTIONS FOR A NEW CARDIAC PACEMAKER

IDS.334 System Design and Management for a Changing World: Projects

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Contents

Executive Summary

Pacemakers, an essential medical device, have significantly evolved over the years, offering innovative solutions for cardiac rhythm disorders. The demand for pacemakers is on the rise due to various reasons including the advancements in pacemaker technology and are becoming more accessible and effective. While current pacemaker technology has significantly improved patient outcomes, limitations related to lead complications, battery life, and invasiveness remain. The evolving nature of medical technology landscape combined with shifts in patient needs introduce uncertainties in long-term device performance and market demand. This project outlines the development program of a next-generation pacemaker, that incorporates a new state of the art energy harvesting technology that increases the overall longevity of the device that allow this product to compete favorably in a relatively mature market.

The current stage of this technology was explored to better understand its maturity level and market demand. Medtronic, Abbott, and Boston Scientific are leading manufacturers of pacemakers in the US, driving innovation to enhance patient care and improve quality of life. As pacemakers are surgically implanted, their longevity is crucial, as any replacement or maintenance requires additional surgery. Future developments in this technology are expected to focus on finding alternative battery or power sources to extend device lifespan. Potential solutions include developing more energy-dense batteries, implementing intelligent power management, and exploring experimental energy harvesting technologies like harvesting energy from the body's movements or temperature differences.

The goal of this project is to explore the overall development program and commercialization trajectory of a next-generation pacemaker equipped with a new state-of-the-art energy harvesting power technology [6]. A baseline model was developed to simulate the entire development cycle, from initial R&D to commercialization. Five uncertainties were incorporated into the model to assess potential outcomes and risks. These uncertainty parameters were selected based on my own industry experience as well as from my research of this technology. A sensitivity analysis was conducted on the model, varying uncertain parameters to assess their impact on overall outcomes. Flexibility was incorporated into the design to mitigate risks and optimize the potential for high-value outcomes.

Scenario 4, which incorporates multiple forms of flexibility is the recommended approach. This scenario minimizes the overall value at risk by 135% and significantly improves the value at gain by 35% and increases the overall NPV average by 46%. Overall, this scenario confirms the viability of this investment as it demonstrates a significantly positive NPV across a wide range of probable outcomes which can be translated as long-term viability and success of this new pacemaker technology in a dynamic and uncertain future.

Background

A cardiac pacemaker is a small, implantable bio-electronic device that helps regulate the heart's rhythm [1][2][3][4][5]. It's designed for individuals with heart rhythm disorders, specifically those experiencing bradycardia (slow heart rate) or irregular heartbeats [3]. The pacemaker mimics the function of the heart's natural pacemaker, the sinus node, ensuring the heart maintains a steady and healthy beat [1][2][3][4]. This is crucial because a slow or erratic heartbeat can lead to symptoms like dizziness, shortness of breath, fatigue, and even fainting and in severe cases, it can be life-threatening.

The basic design of a traditional pacemaker consists of two main components: the pulse generator and the leads, see Figure 1[1][2][4]. The pulse generator is a small metal box containing a battery and electronic circuits.[2] It controls the rate and timing of electrical impulses sent to the heart.[1][2] Leads are insulated wires that connect the pulse generator to the heart.[2] One to three leads are typically used, depending on the type of pacemaker and the patient's specific needs. These leads are placed in the heart's chambers and transmit the electrical signals that regulate the heartbeat [1][2][4].

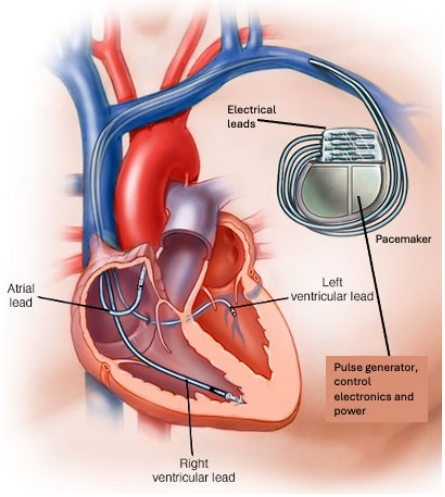


Figure 1: Implantable Cardiac Pacemaker

Image source: https://www.mayoclinic.org/tests-procedures/pacemaker/multimedia/pacemaker/img-20008517

The concept of electrically stimulating the heart dates back to the late 1800s. However, the first implantable pacemaker, developed in the 1950s, was a bulky, external device. Subsequent advancements led to smaller, more reliable, and longer-lasting pacemakers powered by lithium batteries. More recent innovations include leadless pacemakers, rate-responsive pacemakers that adjust to the body's activity level, and pacemakers that can monitor and diagnose other heart conditions. Current innovations in pacemaker technology continue to push the boundaries of cardiac care. Leadless pacemakers offer a less invasive alternative to traditional devices, reducing the risk of infection and lead complications. Remote monitoring technology allows physicians to check pacemaker function and adjust settings without in-office visits. Furthermore, researchers are exploring new energy sources for pacemakers, such as body motion or glucose, to potentially eliminate the need for battery replacements.

Several companies are at the forefront of pacemaker development and manufacturing. These include Medtronic, Abbott, and Boston Scientific. The rising demand for pacemakers translates to a large market opportunity and potential for significant revenue generation, see Figure 2. North America currently dominates the market, due to advanced healthcare infrastructure, high healthcare spending, and favorable reimbursement policies [8][9]. While North America leads the market, the Asia Pacific region is expected to witness the fastest growth in the

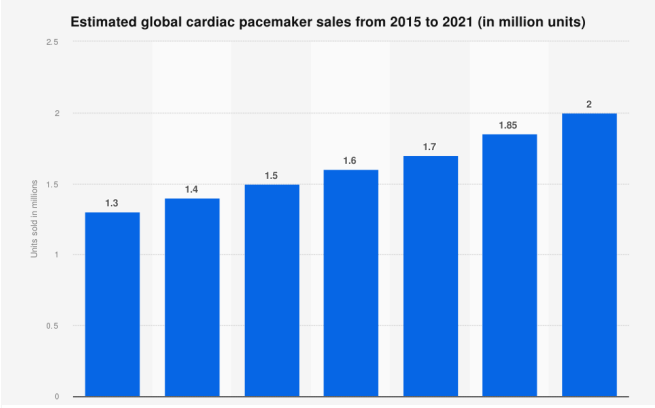


Figure 2 Pacemaker market landscape

Image source: https://www.statista.com/statistics/731763/cardiac-pacemaker-units-sales-worldwide/

coming years. This growth is attributed to increased healthcare investments, particularly in countries like China, Japan, and India, and greater penetration by key market players into the region's untapped potential [8][9]. The market is further segmented by product type, with implantable pacemakers holding the largest share, followed by external pacemakers. Within implantable pacemakers, single-chamber, dual-chamber, biventricular, conventional, and leadless devices cater to diverse patient needs. As the market matures further, ongoing innovations and increasing accessibility to advanced technologies are expected to shape the future of cardiac pacing and drive market expansion in various regions globally.

The typical development cycle of an implantable bio-electronic device such as the pacemaker can take anywhere from 5 to 7 years. A typical product development process at a very high level consists of four major phases, concept and feasibility phase, design and development phase, clinical trials and FDA approval phase, and launch / commercialization phase (Figure 3). In the concept and feasibility phase, we identify clinical needs and the target patient population by analyzing existing technology, pinpointing limitations, and exploring potential improvements. Then, preliminary designs and proof-of-concept prototypes are developed. Following this, initial laboratory and in-vitro tests are conducted to assess the feasibility and safety of the proposed design. The design and development phase involves refining the pacemaker's hardware and software components, optimizing performance, and ensuring manufacturability. Preclinical testing, typically conducted on animal models, evaluates the device's safety and efficacy, including lead performance, pacing algorithms, and battery life. Design verification and validation testing ensures the pacemaker meets design specifications and performs as intended. The Clinical Trials and FDA approval phase generally involves filing applications and submitting required data and reports to the FDA for their evaluation. The FDA reviews these submissions and either approves the device or request additional information. This is what adds additional uncertainty to the overall time for this FDA clearance process. After approval, manufacturers scale up production, launch the product, and implement post-market surveillance to monitor device performance and safety.

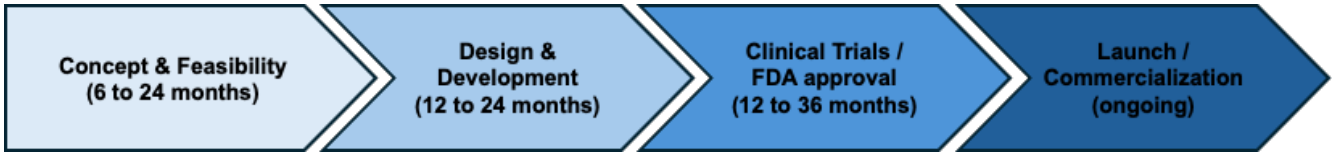


Figure 3 High-level product development process for medical devices

Disclaimer

This work is a product of an academic exercise for the purposes of developing a class project for IDS 334, System Design and Management for a changing world: projects course in Fall 2024. It is intended for educational purposes only. It does not represent a comprehensive or definitive analysis of the proposed product or technology.

System Model

Model Walkthrough / Information Flow

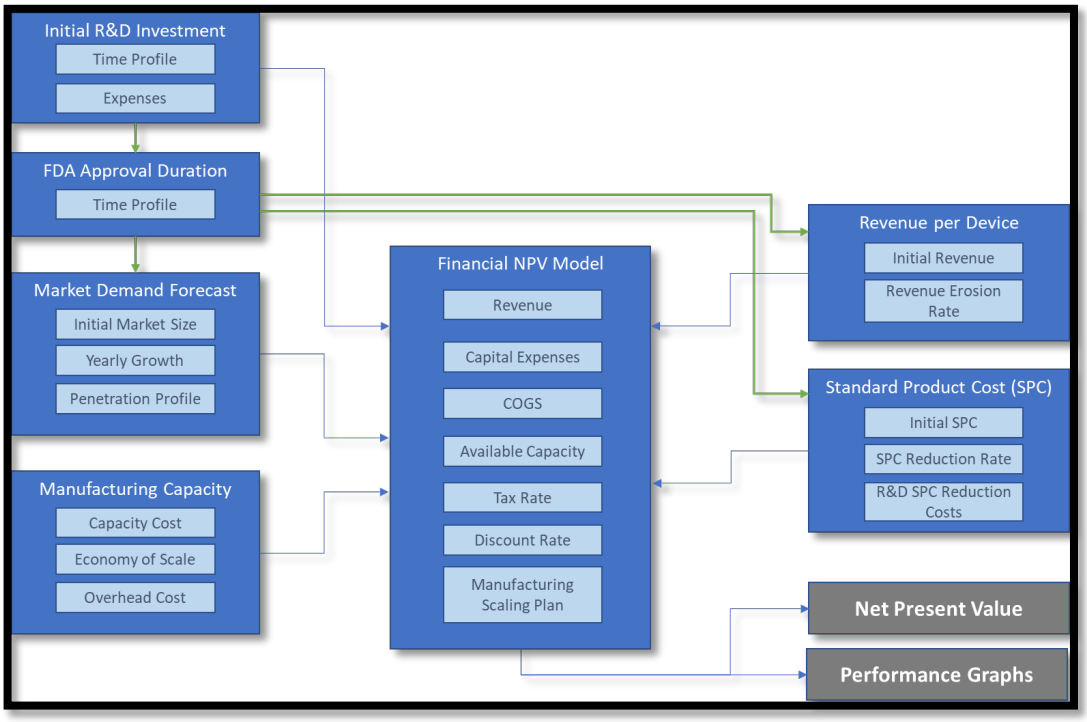


Figure 4 Baseline Static Model Information Flow

A comprehensive Excel-based system model was developed to simulate the entire product development and commercialization process of a new cardiac pacemaker. Figure 4 provides an overview of the model's information flow. At a high level, the model consists of six interconnected sub-models that simulate key aspects of the overall process:

Sub-Model-R&D Investment Profile: Sub-model focused on the initial R&D time and expense associated with developing this new pacemaker device. Inputs: Durations for R&D Phases, Expenses for R&D Phases. Outputs: Yearly Expenses

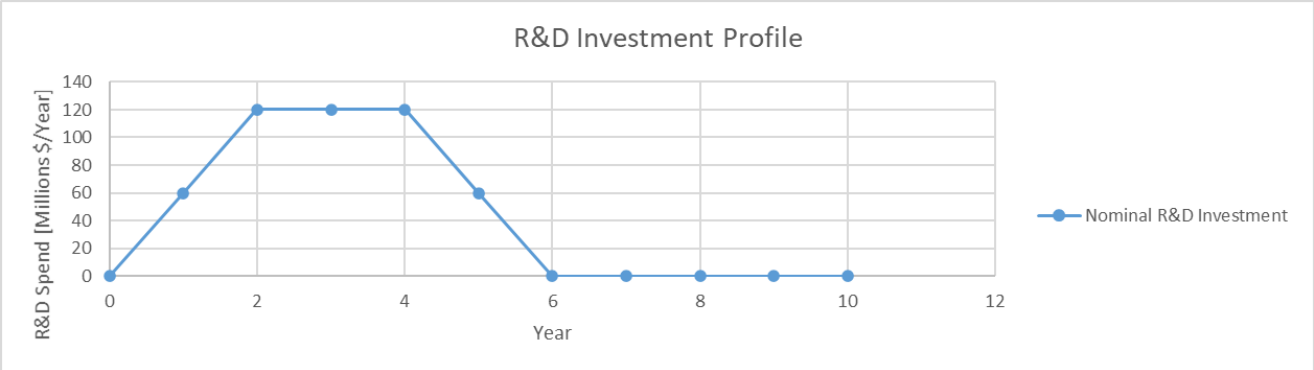


Figure 5 Sub-Model Output: Sample R&D Investment vs Time

Sub-Model-FDA Approval Duration: Focuses on how much time will pass from the completion of R&D to when the FDA would approve the device for general use. Inputs: R&D Completion Time, FDA Duration Outputs: Market Approval Time

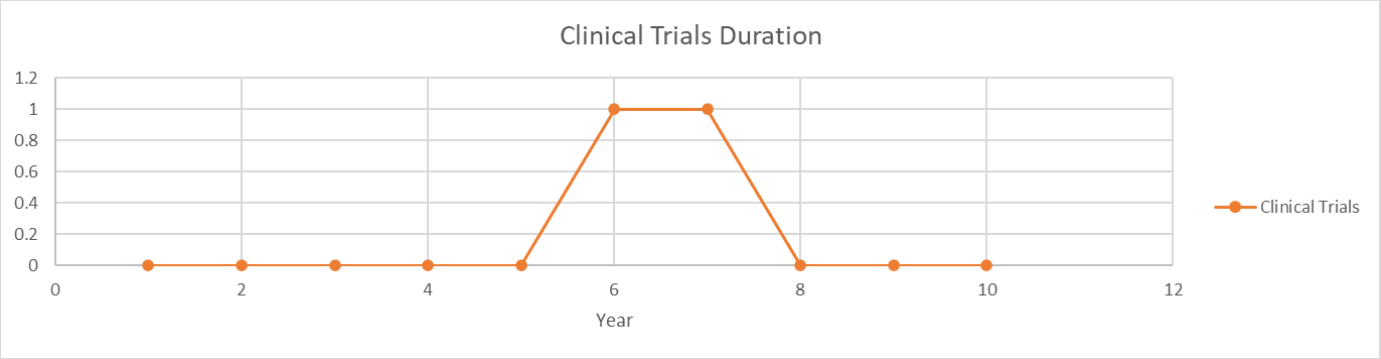


Figure 6 Sub-Model Output: Clinical Trials Duration vs Time

Sub-Model-Forecasted Demand Curve: Focuses on what the addressable market size is and how much the new pacemaker device would be able to capture. Inputs: Initial Market Size, Market Growth Rate, Expected Penetration. Outputs: Yearly Actual Demand for new pacemaker.

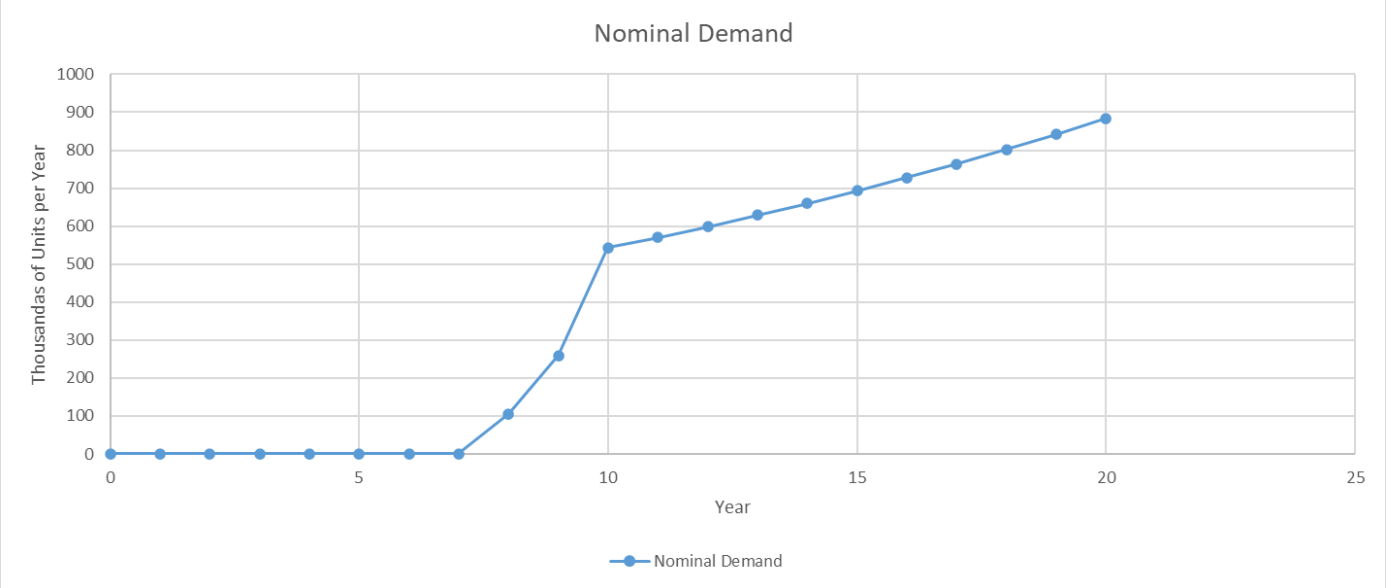


Figure 7 Sub-Model Output: Nominal Demand vs Time

Sub-Model-Manufacturing Capacity: Focuses on the relationship between the Scale of the pacemaker factory and the cost / overhead of the factory. Inputs: Capacity Unit Cost, Economy of scale factor, Overhead unit cost.

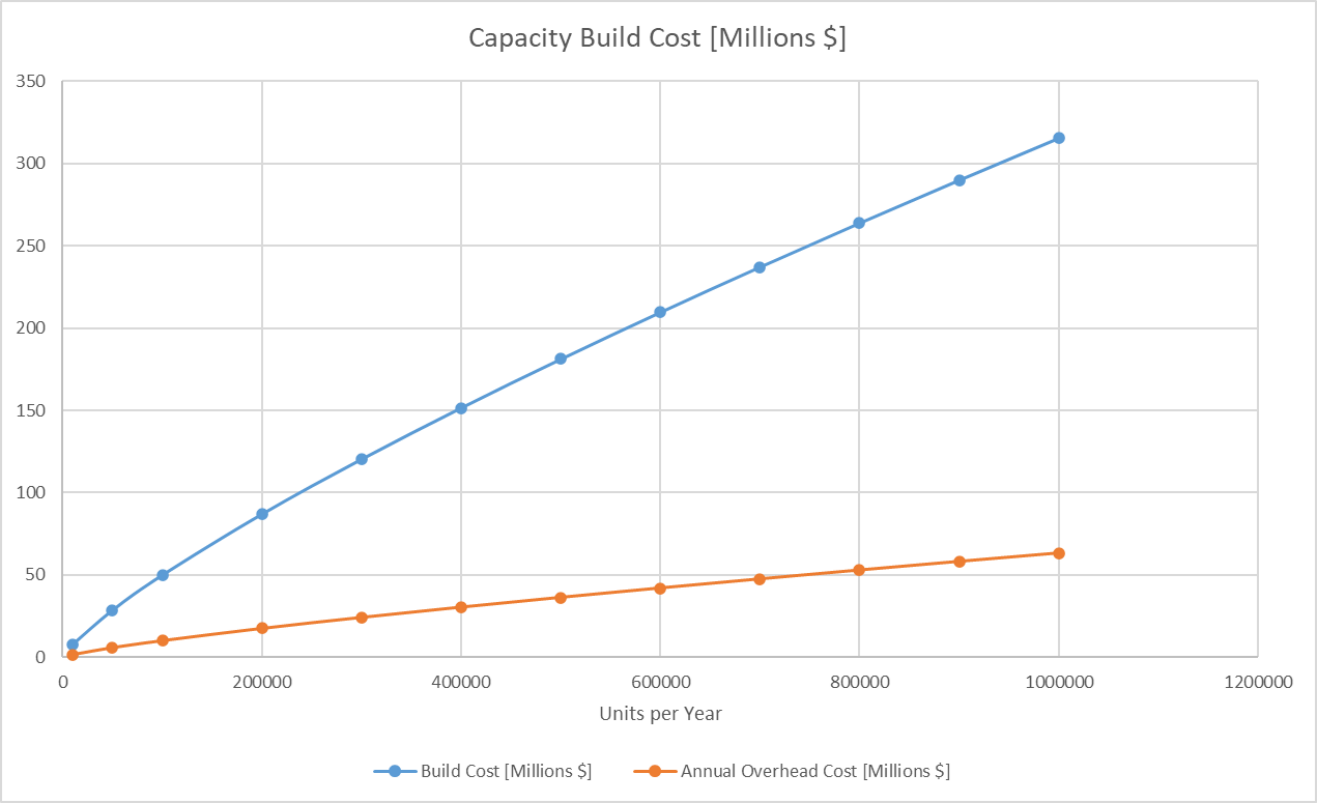


Figure 8 Sub-Model Output: Manufacturing & Upkeep Cost vs Scale

Sub-Model-Revenue per Device: Focuses on the expected revenue per individual unit over time. Inputs: Initial Revenue per unit, Revenue Erosion Rate Outputs: Yearly Revenue per unit

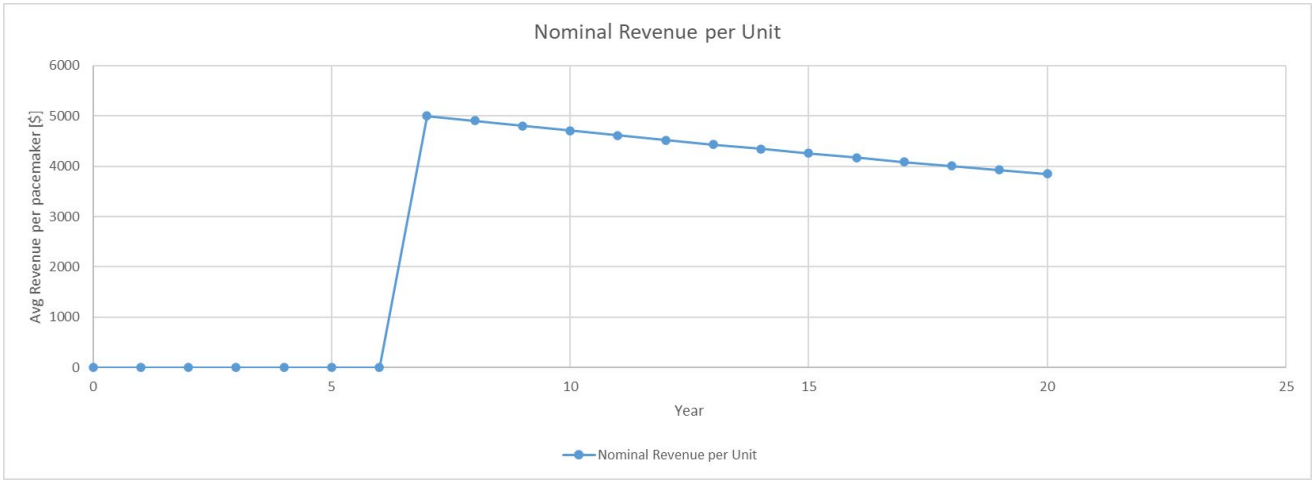


Figure 9 Sub-Model Output: Unit Revenue vs Time

Sub-Model-Standard Product Cost (SPC) per Device: Focuses on the expected material and labor costs associated with producing a pacemaker. Also models the expected improvement in SPC via incremental R&D spend Inputs: Initial SPC per unit, SPC Improvement Rate, R&D Expense Outputs: Yearly Revenue per unit

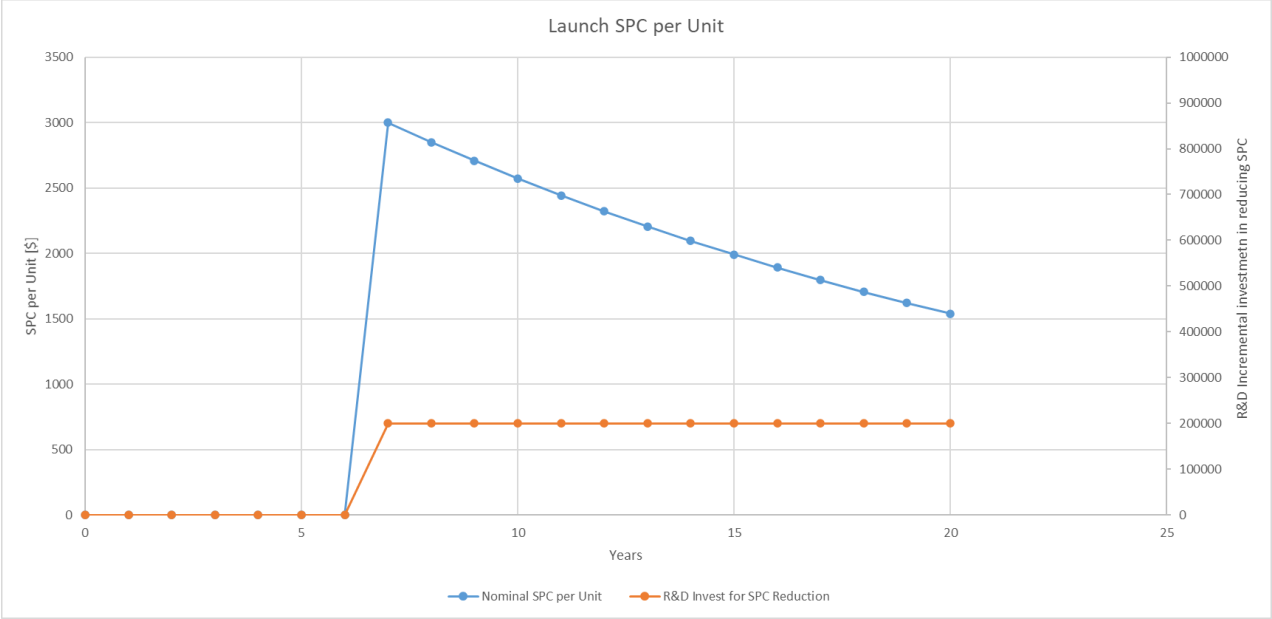


Figure 10 Sub-Model Output: Unit SPC and Incremental R&D expense vs Time

The outputs of these six sub-models are used as input for the overall financial NPV model. Additional input for the financial NPV model are: Discount Rate, Tax Rate, and Factory Build Plan. This part of the model also tracks the overall size of the factory and how many pacemakers can be produced. It calculates on a yearly basis: Units Produced, Revenue, Capital Expense, Cost of Goods and Services (COGS), Taxes, Cash Flow, Discounted Cash Flow, and Cumulative Value. It outputs an overall NPV for the scenario and provides several figures to show they dynamics of what is happening over time. An example of these output can be found in Figure 19 in the following section.

Uncertainty Parameters

Several factors can complicate large-scale projects. For the pacemaker project, the following five factors were deemed most significant:

- **Yearly R&D Expenditure**: This is the amount of money spent on the initial development of the pacemaker on a yearly basis over the course of 5-year development timeline. It's very common in the development of new complex engineering projects to have miss-estimates in the labor and direct expenses needed. This uncertainty was modeled as a 30% deviation per year from nominal in a uniform distribution. The impact of this risk is the overall expenditure in the early phase of the products lifetime.

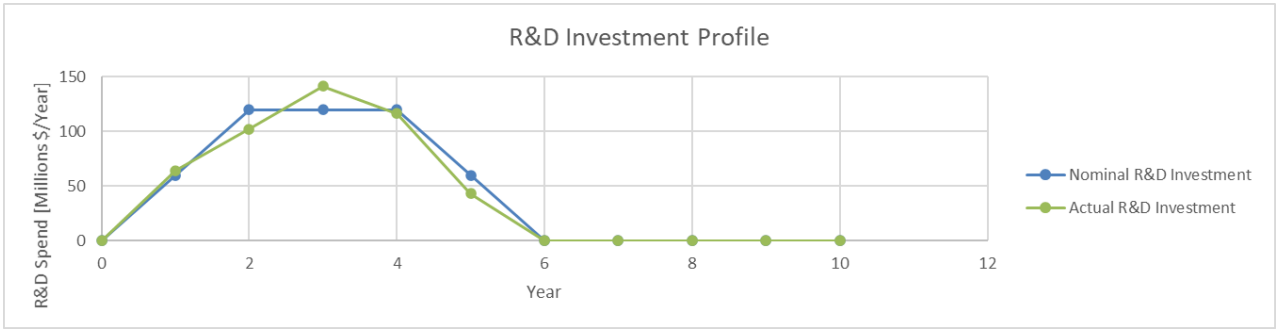


Figure 11 Example of Nominal vs Actual R&D Expense

- **Clinical Trials Duration**: This is the time it will take after R&D development is complete for clinical trials data to be collected and the FDA to approve the new cardiac pacemaker device for general use by the public. Since this application involves a high risk to human health, the regulatory hurdles are very high and it's quite common for approval to be held up for more data to review. This uncertainty was modeled as a 1-3 year with a uniform distribution. As clinical trials get delayed, it impacts the overall time period in which the product is competitive, when revenue can start to be recognized, and when you might want to start building your factory capacity.

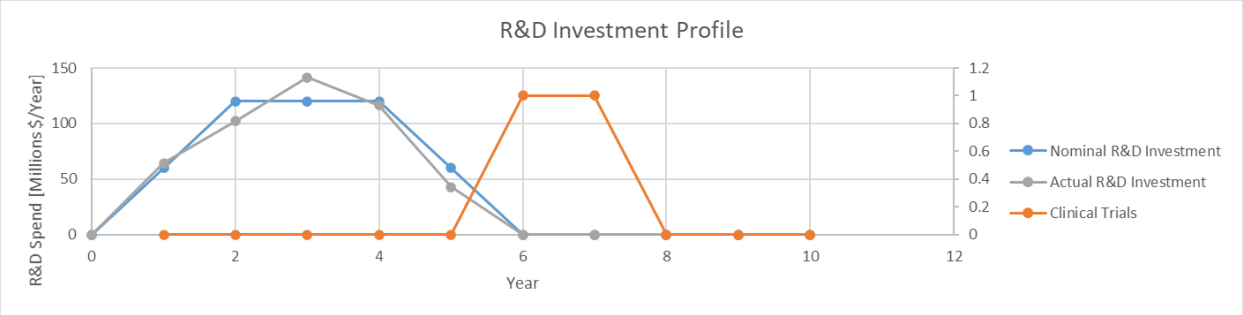


Figure 12 Example of clinical trials duration.

- **Volatility of Demand Growth:** This is the year over year volatility in the expected growth in demand of the pacemaker market. Generally, this encompasses all the factors that might impact how the market changes overtime, but specifically the biggest risks might come from alternate medical technologies or therapies that reduce the need for patients to need cardiac pacemakers. This uncertainty was modeled as a 30% deviation per year from nominal in a uniform distribution.

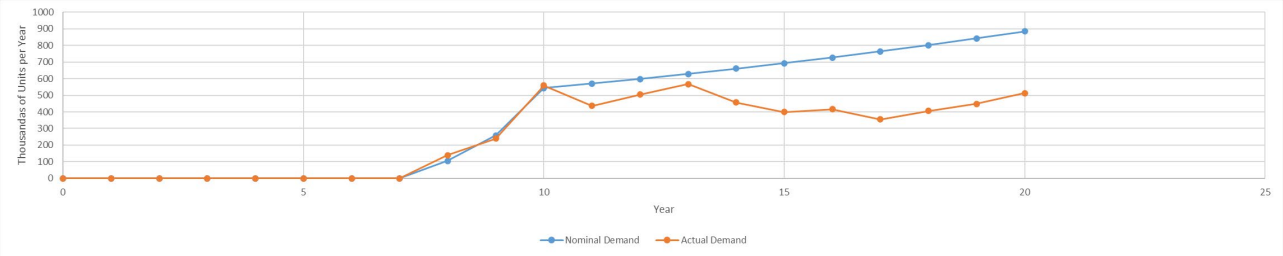


Figure 13Example of nominal vs actual product demand

- **Supply Chain Volatility:** This is the impact of Supply Chain Volatility on the SPC (Standard Product Cost) of the pacemaker. This is capturing the unknown impacts of raw material pricing, storage, shipping, and sub-supplier technical issues that are common for mass market products. This uncertainty was modeled as a 36% deviation per year from nominal in a uniform distribution.

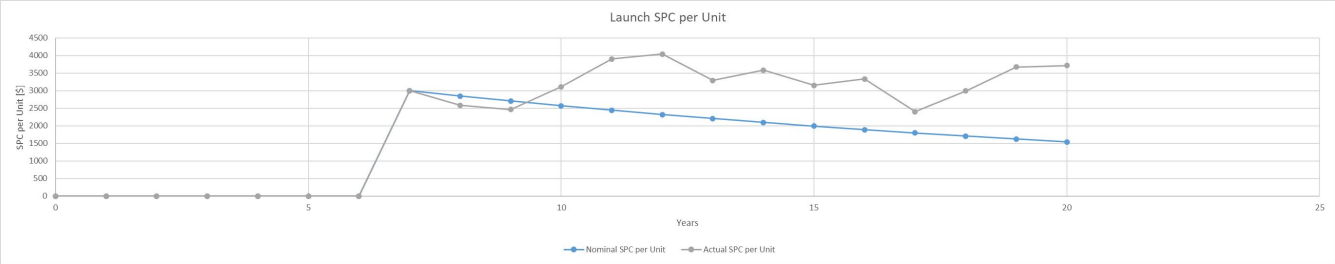


Figure 14 Example of nominal vs actual unit SPC

- **<u>Per Unit Revenue Volatility</u>**: This is the uncertainty related to how much revenue would be recognized from selling a single pacemaker on average. The source of this would be driven mostly by pricing negotiations with large medical networks, insurers, and government entities as is common for implantable devices This uncertainty was modeled as a 10% deviation per year from nominal in a uniform distribution.

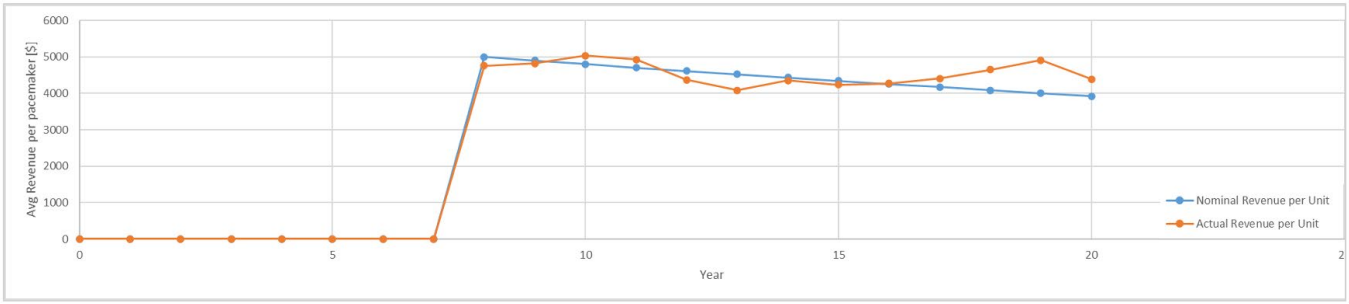


Figure 15 Example of nominal vs actual unit revenue

Figure 16 presents the overall data flow in the model, incorporating various sources of uncertainty. These uncertainties are represented by uniform probability density functions within defined value ranges. Excel's built-in random number generator functions are utilized to simulate these uncertainties.

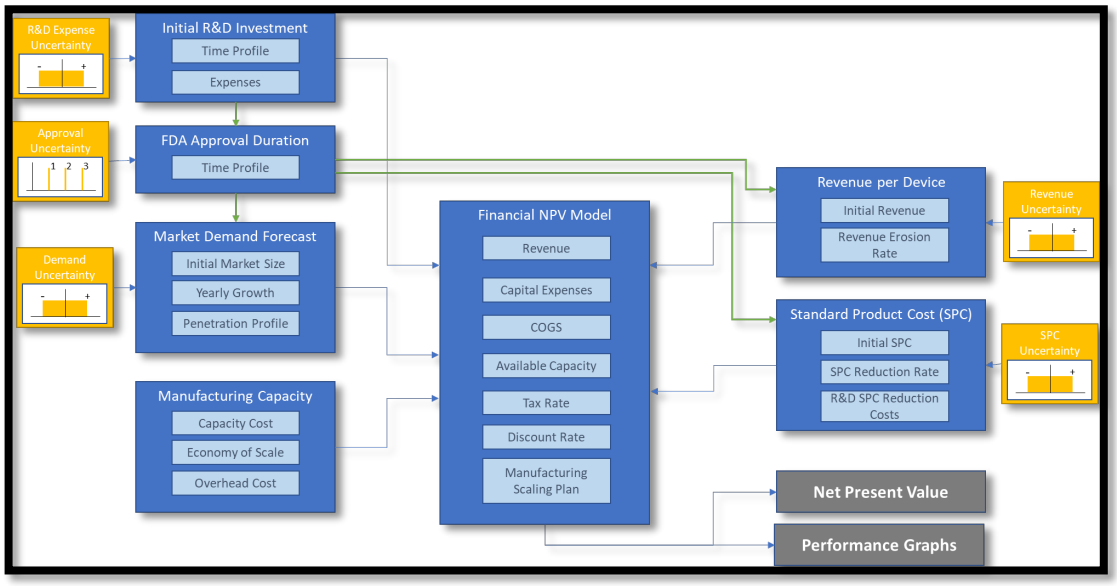


Figure 16 Uncertainty Model Information Flow

A Monte Carlo simulation was used to generate a distribution of potential outcomes based on the identified uncertainties. To facilitate this, the "What-If Data Table" function in Excel was utilized to run the model thousands of times. Figure 17 below illustrates the workflow of the Monte Carlo simulation in Excel.

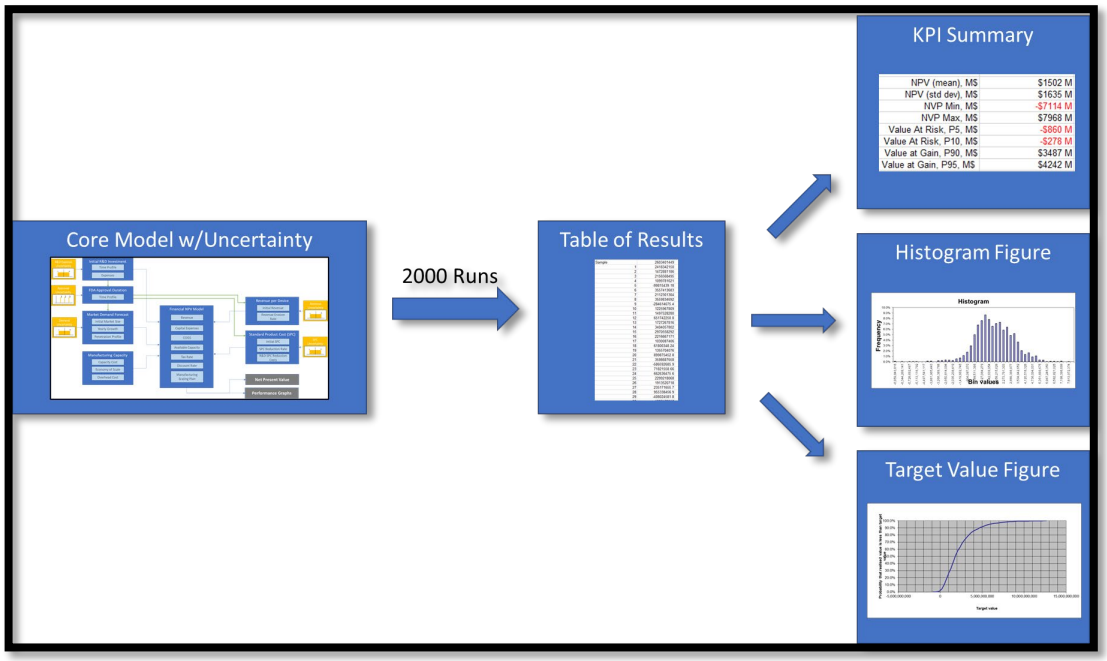
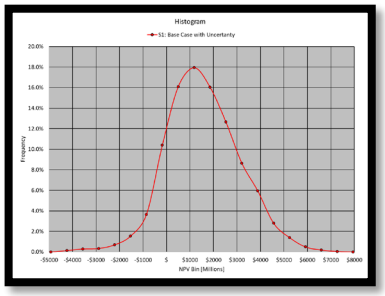


Figure 17 Monte Carlo Simulation Information Flow

Derived Outputs

Each Monte Carlo simulation, based on specific input parameters, generates 2,000 equally likely net present value (NPV) results. To effectively analyze these results, we process the data into various output formats for comparison with other Monte Carlo scenarios. First, we'll summarize the results statistically to obtain quantitative values. Next, we visualize the distribution by binning the results into a histogram. Finally, we calculated the cumulative distribution to generate a target value graph. These three methods helped to compare the performance differences between various distributions.

NPV (mean), M$	$1591 M
NPV (std dev), M$	$1583 M
NPV Min, M$	-$6820 M
NPV Max, M$	$7329 M
Value At Risk, P5, M$	-$626 M
Value At Risk, P10, M$	-$134 M
Value at Gain, P90, M$	$3633 M
Value at Gain, P95, M$	$4273 M



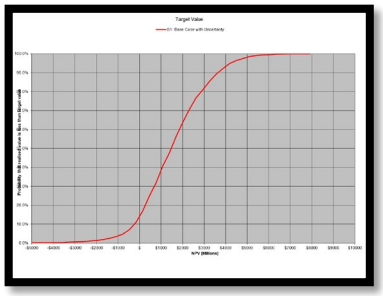


Figure 18Example outputs of Monte Carlo Simulation

Base Cases

Scenario 0: Static Base Case

The deterministic base case uses nominal values for all input parameters in the model and does not include any uncertainty. The factory build plan was optimized to fit the forecasted demand curve and the economy of scale.

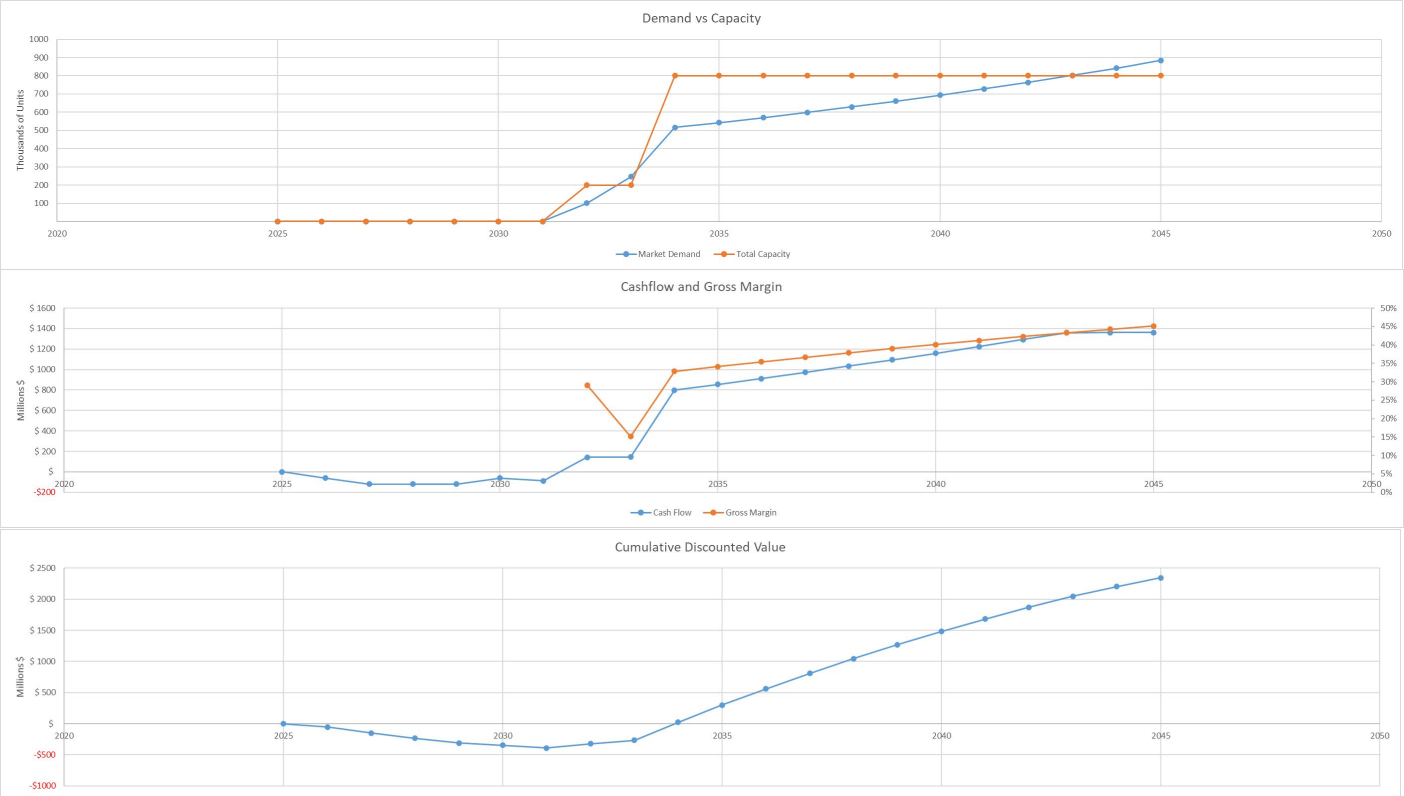


Figure 19: Dynamics of Scenario 0: Static Base Case

With these nominal values, the static base case provides an overall NPV of $2,346 Million over the course of a 20-year outlook.

Quantifying Uncertainty

With a functioning static base case, a sensitivity analysis was performed to understand how each form of uncertainty independently impacts the overall NPV. High and low ranges for all the uncertainties except the clinical trials duration was established by calculating +/- 1 SD of the variation. For the clinical trials duration, the full range was quantized to 1,2, or 3 years. The results were non-intuitive as it was originally expected that the R&D expenses and the clinical trials duration were going to play a much bigger influence. Results showed they were less significant than the factors related to the Supply Chain per unit costs, per unit revenue, and demand forecast. Figure 20 and Figure 21 below illustrate the overall magnitude of the independent uncertainties.

Category	Low (-1SD)	High (+1SD)	Low Result [M$ NPV]	High Result [M$ NPV]	Spread [M$ NPV]
Yearly R&D Expenditure	-17%	17%	$2,095	$1,978	$117
Clinical Trials Duration	1	3	$2,346	$1,701	$645
Volatility of Demand Growth	-17%	17%	-$327	$2,857	$3,184
Per Unit Revenue Volatility	-6%	6%	$305	$4,586	$4,281
Supply Chain Volatility	-21%	21%	$3,792	-$8,387	$12,179

Figure 20 Table of uncertainty ranges and outcomes

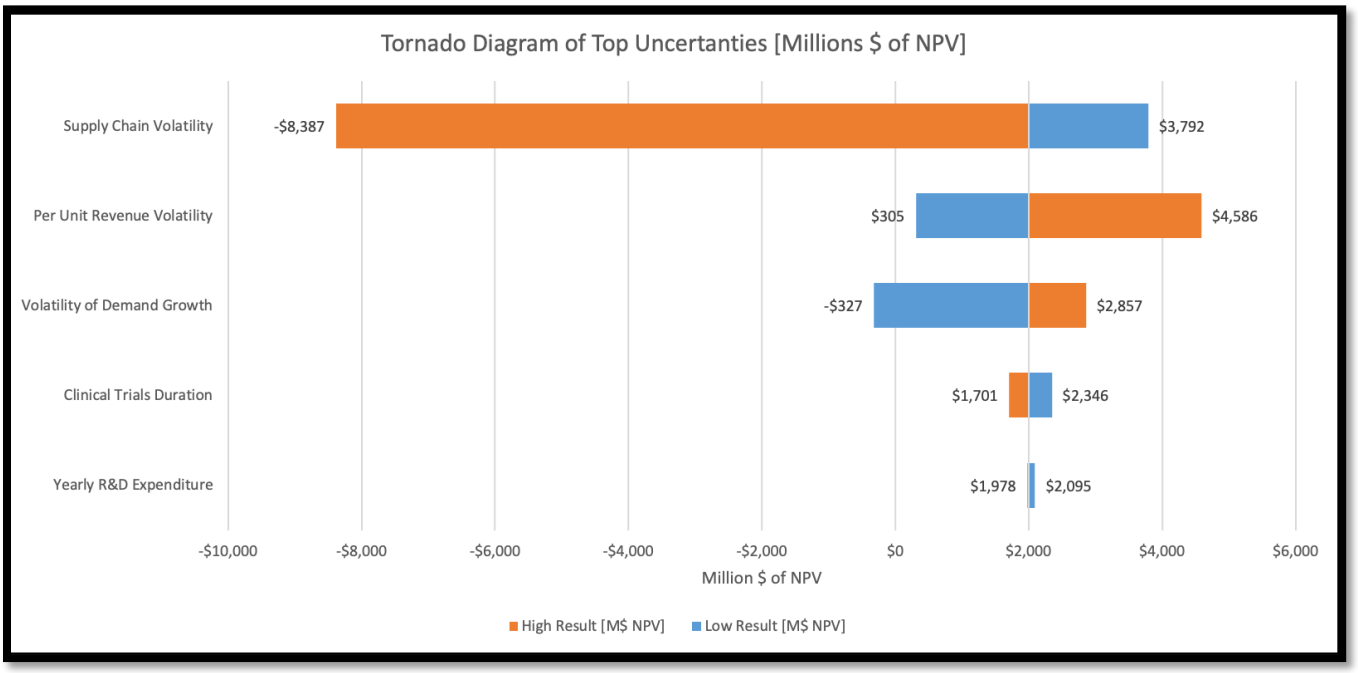


Figure 21 Tornado Diagram showing the independent impact on NPV of each source of uncertainty

Based on these results, flexible mitigations would be later identified to minimize the impact of supply chain costs and demand forecast as they have the biggest downside risks.

Scenario 1: Uncertainty in Base Case

Scenario 1 is the first instance where we are exercising the full set of uncertainty in the model via the Monte Carlo simulation as illustrated in Figure 16 and Figure 17. The results of this are detailed in Figure 22, Figure 23, and Figure 24 below. The impact of the "flaw of averages" can be seen when comparing the mean NPV between scenario 0 and scenario 1. Overall, there was a 33% degradation ($2356M → $1562M) in the NPV when we include all the non-linear impacts of uncertainty. 73% of outcomes when including uncertainty will be worse than the static base case. Moreover, we also see the possibility of significant losses with the worst-case of scenario 1 with minimum NPV of -$7.2B loss and the P5 Value at Risk of -$757M.

KPI	S0: Static Base Case	S1: Base Case with Uncertanty	S1 vs S0
NPV (mean)	$2346 M	$1562 M	-33%
NPV (std dev)		$1635 M	
NPV Min		-$7292 M	
NPV Max		$7613 M	
Value At Risk, P5, $		-$757 M	
Value At Risk, P10, $		-$144 M	
Value at Gain, P90, $		$3620 M	
Value at Gain, P95, $		$4245 M	

Figure 22 Scenario 1: Statistical KPI Comparison

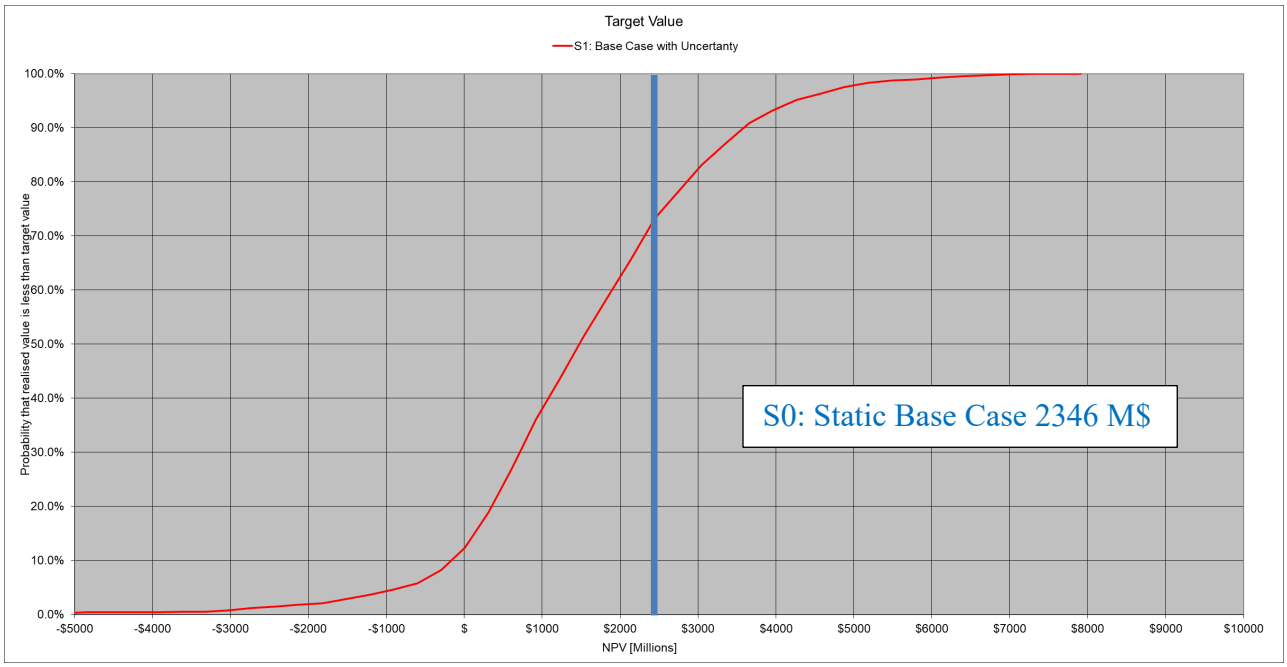


Figure 23 Scenario 1: Target Value Comparison

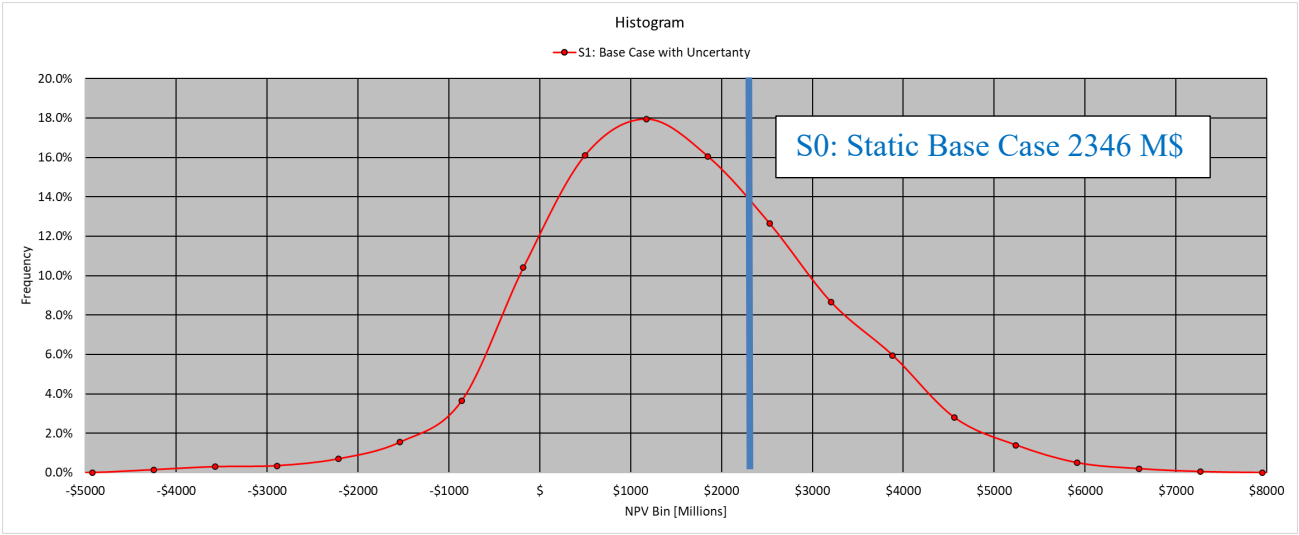


Figure 24 Scenario 1 Results Histogram

Flexible Cases

Scenario 2: Flexible Factory Scaling

To improve the overall performance of the pacemaker program, flexibility was introduced to try to maximize the overall performance and minimize the risk. For scenario 2, new logic was introduced to programmatically decide when and how to scale up factory capacity of the pacemaker factory. Figure 25 below illustrates where this new logic is integrated into the model's information flow.

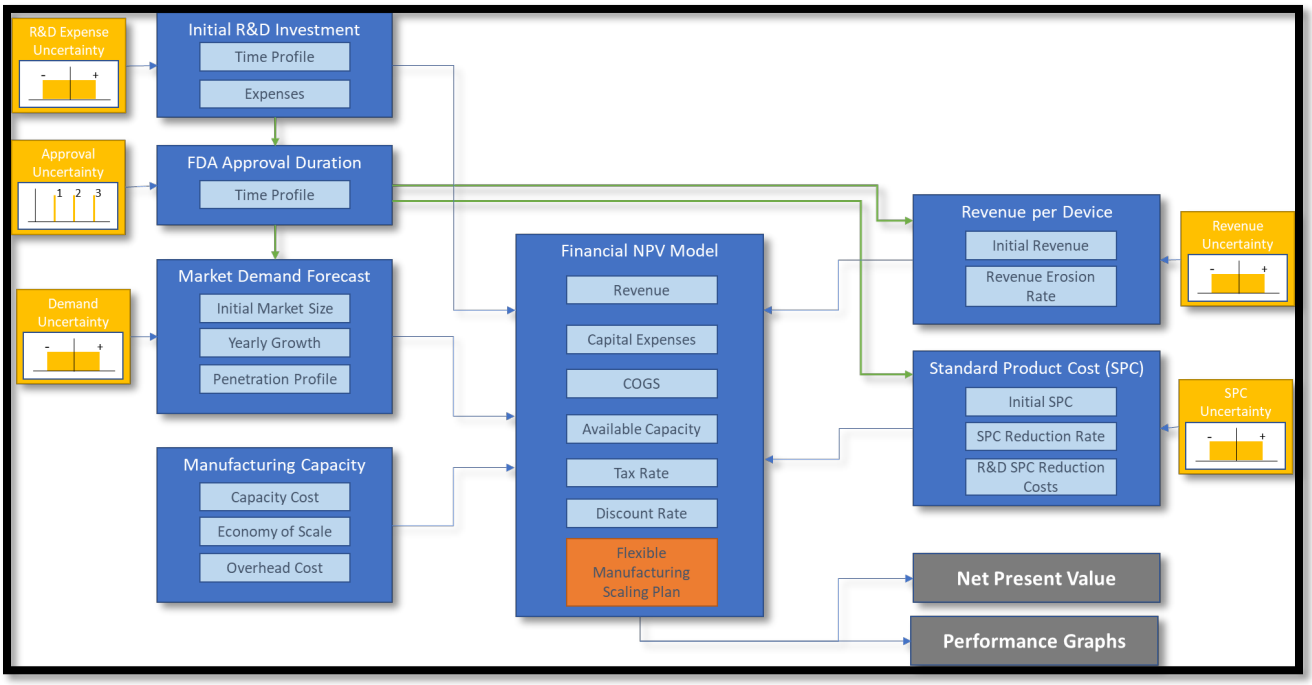


Figure 25 Scenario 2 Uncertainty Model with Scaling Flexibility Information Flow

The Logic of this pacemaker factory scaling flexibility is:

IF ("Last Years Capacity" + "This Years Capacity") < ("Last Years Demand" + "This Years Demand")
THEN IF ("Current Year" <= 2035)
THEN Expand by 400k Units
ELSE Expand by 200k Units
ELSE Do Nothing

This logic is implemented in the excel model as seen in Figure 26. An example of the dynamics of this logic can be seen in Figure 27 where factory expansion is triggered in 2033 (400k Units) and in 2035 (200k Units).

	Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
	Year	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045
[Million $]	R&D Costs	$ 0.0	$ 65.8	$ 85.4	$ 150.6	$ 134.4	$ 45.2	$ 0.0	$ 0.2	$ 85.4	$ 0.2	$ 0.2	$ 0.2	$ 0.2	$ 63.1	$ 27.6	$ 62.7	$ 65.0	$ 71.9	$ 75.4	$ 50.9	$ 43.4
[Thousand	Market Demand	0	0	0	0	0	0	0	0	64	166	408	529	395	498	501	439	353	440	576	458	508
[Thousand	Capacity Addition		0	0	0	0	0	0	0	400	0	0	200	0	0	0	0	0	0	0	0	0
[Million $]	Cost of Addition	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 152	$ 0	$ 0	$ 87	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0
[Thousand	Total Capacity	0	0	0	0	0	0	0	0	0	400	400	400	600	600	600	600	600	600	600	600	600
[Million $]	Overhead Cost	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 30	$ 30	$ 30	$ 42	$ 42	$ 42	$ 42	$ 42	$ 42	$ 42	$ 42	$ 42
[Thousand	Units Produced	0	0	0	0	0	0	0	0	0	166	400	400	395	498	501	439	353	440	576	458	508
[Million $]	COGS	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 324	$ 926	$ 940	$ 879	$ 1413	$ 1187	$ 1150	$ 897	$ 1106	$ 1416	$ 974	$ 1002
[Million $]	Revenue	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 787	$ 1753	$ 1837	$ 1791	$ 2423	$ 2353	$ 1836	$ 1314	$ 1714	$ 2305	$ 1966	$ 2150
[Million $]	Taxable Income	$ 0	-$ 66	-$ 85	-$ 151	-$ 134	-$ 45	$ 0	-$ 0	-$ 237	$ 433	$ 797	$ 780	$ 870	$ 906	$ 1096	$ 582	$ 310	$ 494	$ 772	$ 900	$ 1062
[Million $]	Income Taxes	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 104	$ 191	$ 187	$ 209	$ 217	$ 263	$ 140	$ 74	$ 119	$ 185	$ 216	$ 255
[Million $]	Cash Flow	$ 0	-$ 66	-$ 85	-$ 151	-$ 134	-$ 45	$ 0	-$ 0	-$ 237	$ 329	$ 606	$ 593	$ 661	$ 688	$ 833	$ 442	$ 235	$ 375	$ 587	$ 684	$ 807
[%]	Gross Margin										42%	35%	32%	37%	28%	35%	24%	18%	22%	25%	35%	38%
[Million $]	DCF		-$ 59	-$ 68	-$ 107	-$ 85	-$ 26	$ 0	-$ 0	-$ 96	$ 119	$ 195	$ 170	$ 170	$ 158	$ 171	$ 81	$ 38	$ 55	$ 76	$ 79	$ 84
[Million $]	Cumulative Value	$ 0	-$ 59	-$ 127	-$ 234	-$ 319	-$ 345	-$ 345	-$ 345	-$ 441	-$ 322	-$ 127	$ 43	$ 213	$ 371	$ 541	$ 622	$ 660	$ 715	$ 791	$ 871	$ 954

Figure 26 Pacemaker Factory Scaling logic is implemented in the blue highlighted row in excel.

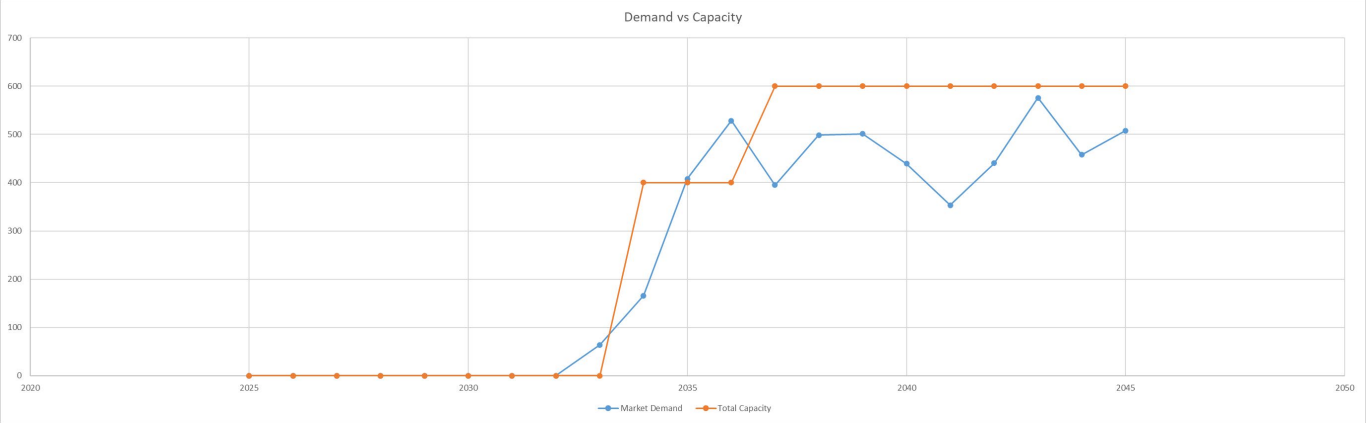


Figure 27 Demand vs Capacity Dynamics Example with flexible scaling logic

With this new factory scaling logic enabled, the entire Monte Carlo simulation was re-run and the results of scenario 2 can be viewed below in Figure 28, Figure 29, and Figure 30. The performance of scenario 2 improved across the board relative to scenario 1 with the biggest magnitude improvements occurring at the high end of the target value curve (NPV Value at Gain P95 improving by $1.3B). The mean improved modestly at 16% and the NPV Value at Risk P5 was improved by $388M cutting loss amount in half.

KPI	S0: Static Base Case	S1: Base Case with Uncertanty	S1 vs S0	S2: Uncertanty Model with Scaling Flexibility	S2 vs S1
NPV (mean)	$2346 M	$1562 M	-33%	$1814 M	16%
NPV (std dev)		$1635 M		$1975 M	21%
NPV Min		-$7292 M		-$5233 M	-28%
NPV Max		$7613 M		$13160 M	73%
Value At Risk, P5, $		-$757 M		-$396 M	-48%
Value At Risk, P10, $		-$144 M		-$43 M	-70%
Value at Gain, P90, $		$3620 M		$4366 M	21%
Value at Gain, P95, $		$4245 M		$5523 M	30%

Figure 28 Scenario 2: Statistical KPI Comparison

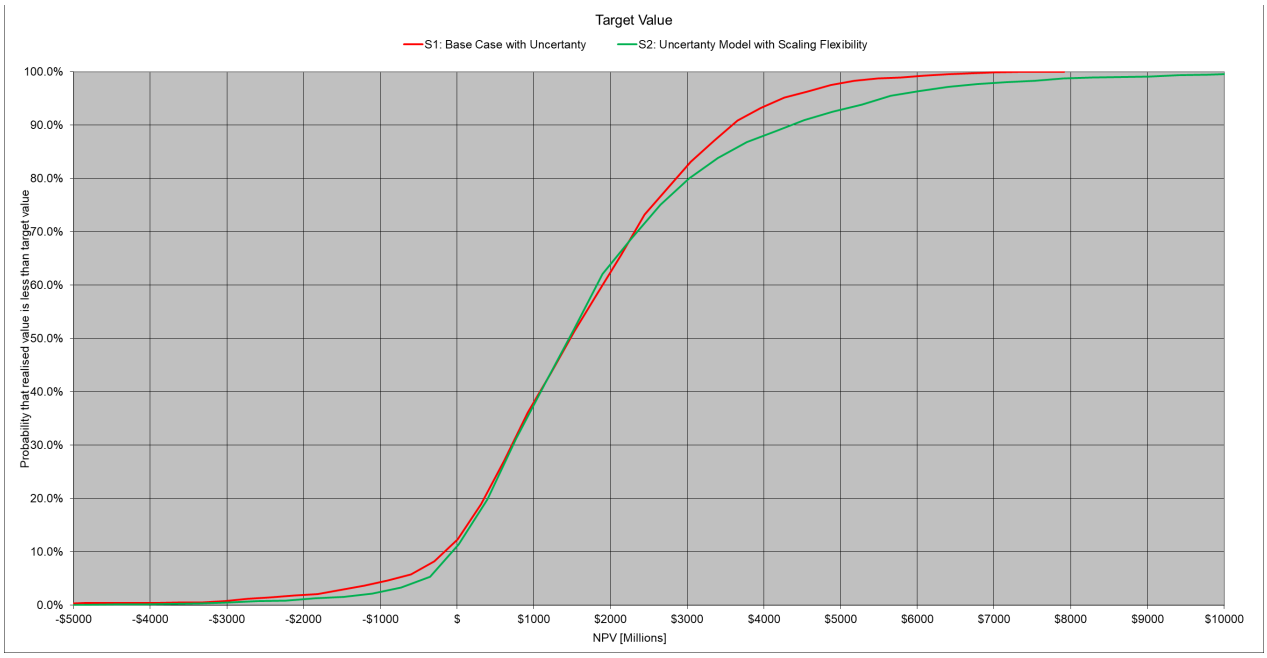


Figure 29 Scenario 2: Target Value Comparison

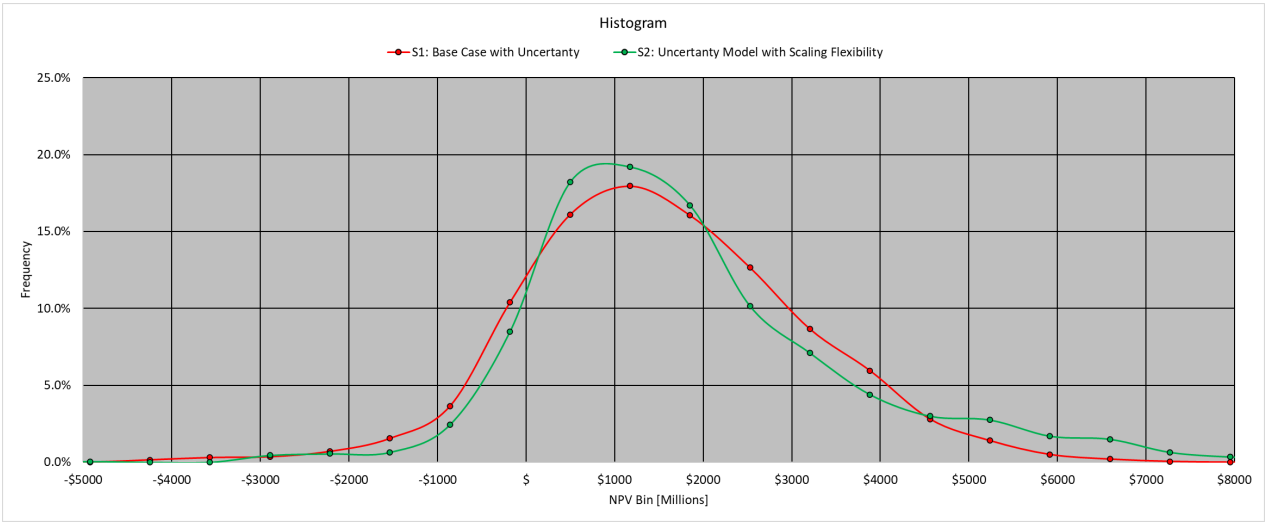


Figure 30 Scenario 2: Histogram Comparison

S3: Flexible SPC

While scenario 2 in the previous section offered a significant improvement over scenario 1, it did not really address the largest driver of negative NPV which is supply chain costs. To mitigate the impact of out-of-control SPC for scenario 3, new logic was introduced to programmatically decide to invest in continuing engineering activities that would improve the SPC of the pacemaker. Figure 31 below illustrates where this new logic is integrated into the model's information flow.

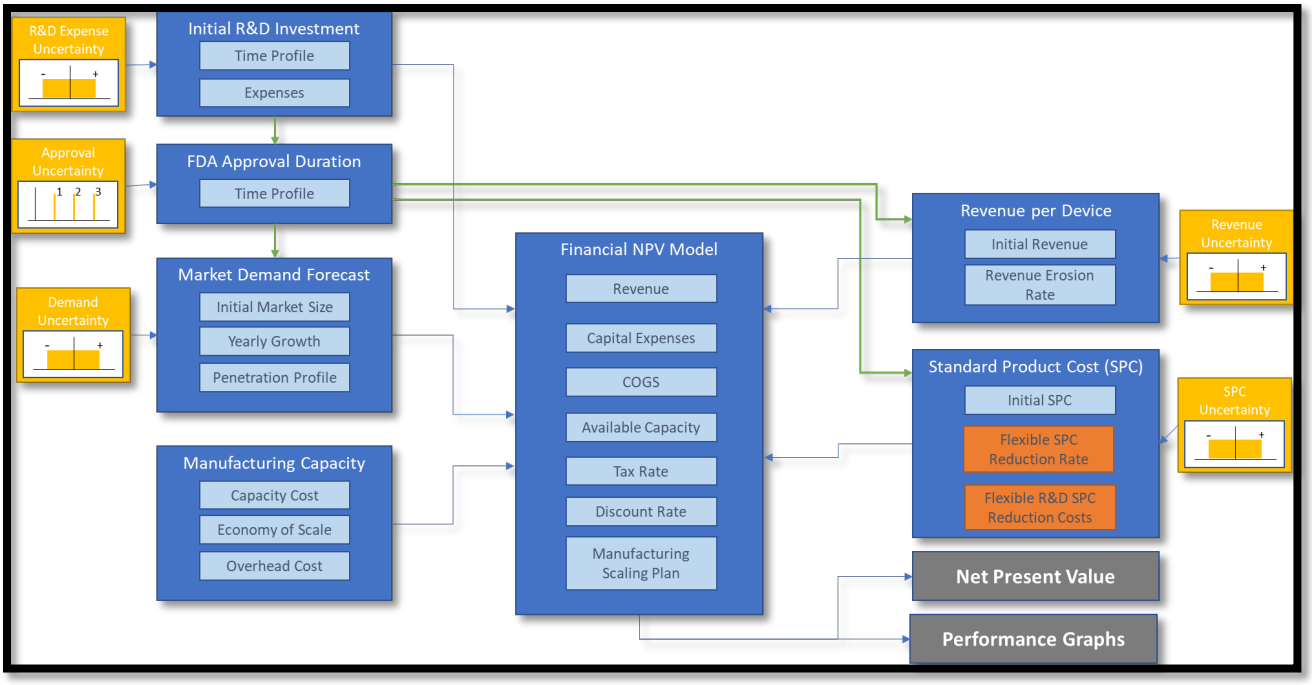


Figure 31 Scenario 2 Uncertainty Model with SPC Flexibility Information Flow

The Logic of this SPC flexibility is:

IF ("Current SPC" – "Forecast SPC" > 10% of Forecast SPC)
THEN Invest is SPC Reduction to be realized in the following year.
ELSE Do Nothing

This investment is parameterized based on how much the current SPC has deviated from the forecast and can only be partially effective. It's quite expensive and it cannot be used to preemptively drive the SPC lower. This logic is implemented in the excel model as seen in Figure 32. An example of the dynamics of this logic can be seen in Figure 33 where R&D investment is triggered several times to mitigate the actual SPC overage vs nominal.

Year	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Nominal SPC per U	0	0	0	0	0	0	0	3000	2850	2708	2572	2444	2321	2205	2095	1990	1891	1796	1706	1621	1540
Actual SPC per Un	0	0	0	0	0	0	0	3000	2142	2548	3283	2932	3323	1872	2150	2498	1923	1919	2341	2579	2368
% Deviation from P	0%	0%	0%	0%	0%	0%	0%	0%	-25%	-6%	28%	20%	43%	-15%	3%	26%	2%	7%	37%	59%	54%
Deviation	0	0	0	0	0	0	0	0	-708	-160	711	488	1002	-333	55	508	32	122	635	958	828
Next Year Reductic	0	0	0	0	0	0	0	0	0	0	355	244	501	0	0	254	0	0	317	479	414
R&D Reduciton Co	0	0	0	0	0	0	0	0	0	0	71087552	48831191	100183551	0	0	50767479	0	0	63468353	95815415	82811354
R&D Invest	0	0	0	0	0	0	0	200000	200000	200000	71287552	49031191	100383551	200000	200000	50967479	200000	200000	63668353	96015415	83011354

Figure 32 Pacemaker SPC Flexibility logic is implemented in the blue highlighted row in excel.

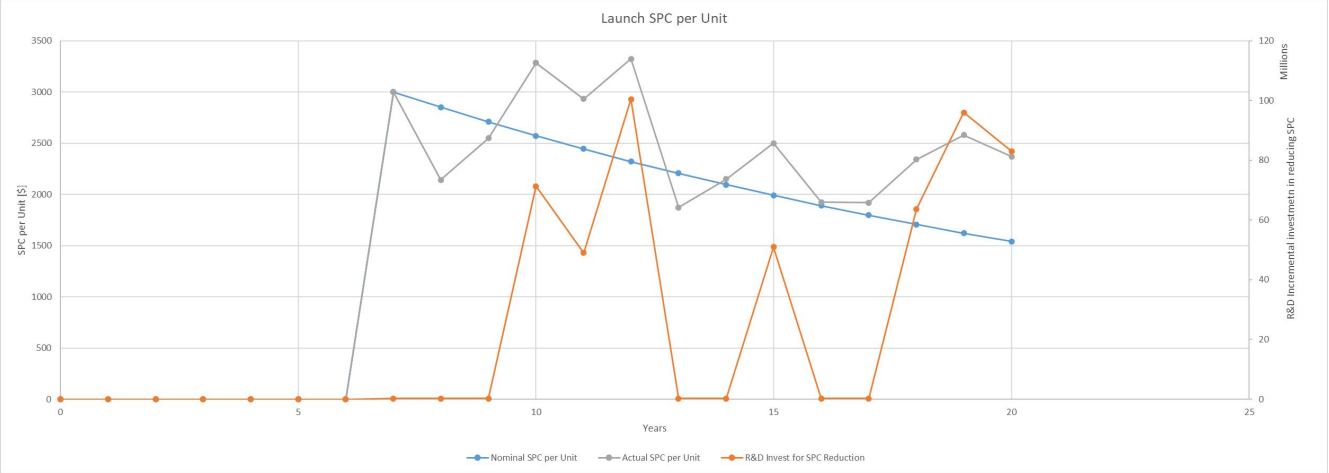


Figure 33 Nominal SPC vs Actual SPC vs R&D Expense Dynamics Example w/ flexible SPC logic

With this new pacemaker SPC logic enabled, the entire Monte Carlo simulation was re-run and the results of scenario 3 can be viewed below in Figure 34, Figure 35, and Figure 36. The performance of scenario 3 improved significantly at the low end of the target value curve relative to scenario 1. The NPV Value at Risk P5 was improved by $892M (118%) pushing it out the net loss territory. The mean improved modestly at 24% and the NPV Value at Gain P95 did not improve meaningfully. Overall, this flexibility significantly reduced the risk to the pacemaker program.

KPI	S0: Static Base Case	S1: Base Case with Uncertanty	S1 vs S0	S2: Uncertanty Model with Scaling Flexibility	S2 vs S1	S3: Baseline with SPC Flexibility	S3 vs S1
NPV (mean)	$2346 M	$1562 M	-33%	$1814 M	16%	$1932 M	24%
NPV (std dev)		$1635 M		$1975 M	21%	$1281 M	-22%
NPV Min		-$7292 M		-$5233 M	-28%	-$905 M	-88%
NPV Max		$7613 M		$13160 M	73%	$6800 M	-11%
Value At Risk, P5, $		-$757 M		-$396 M	-48%	$135 M	-118%
Value At Risk, P10, $		-$144 M		-$43 M	-70%	$393 M	-372%
Value at Gain, P90, $		$3620 M		$4366 M	21%	$3681 M	2%
Value at Gain, P95, $		$4245 M		$5523 M	30%	$4244 M	0%

Figure 34 Scenario 3: Statistical KPI Comparison

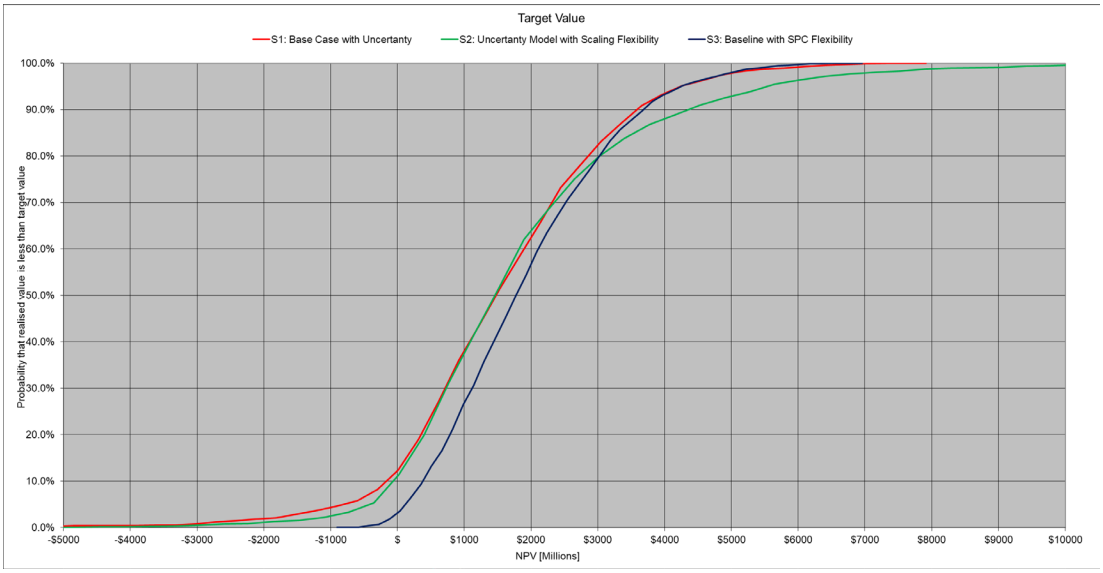


Figure 35 Scenario 3: Target Value Comparison

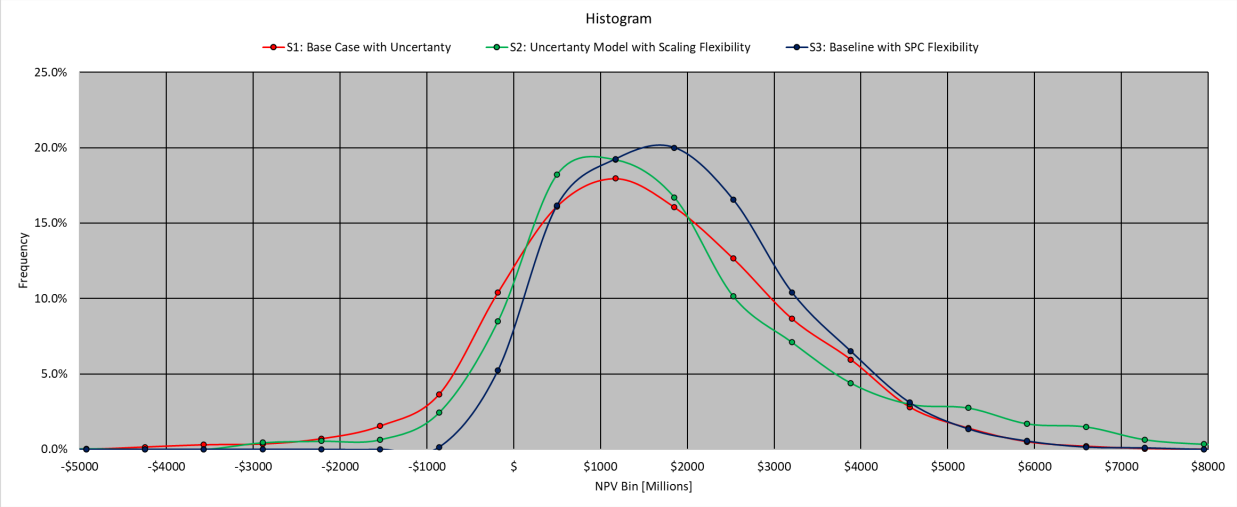


Figure 36 Scenario 3: Histogram Comparison

S4: Flexible Factory Scaling & Flexible SPC Scaling

The results of scenario 2 and 3 are very complementary to each other in the target curve domain. Scenario 2 improves the high end of the curve maximizing the Value at Gain and scenario 3 improves the low end of the curve improving the Value at Loss. Scenario 4 combines the flexible logic of both previous scenarios to demonstrate this synergy and show that there is not unexpected competing dynamics. Figure 37 below illustrates where the combination of this logic integrated into the model's information flow.

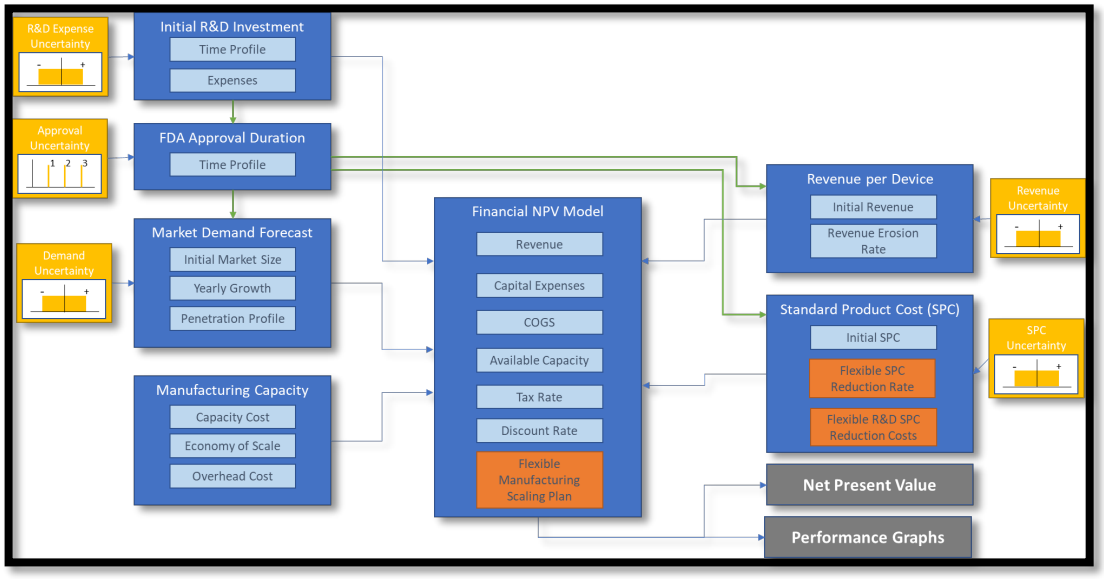


Figure 37 Scenario 3 Uncertainty Model with Scaling and SPC Flexibility Information Flow

With both the flexible factory scaling logic and flexible SPC logic enabled, the entire Monte Carlo simulation was re-run and the results of scenario 4 can be viewed below in Figure 38, Figure 39, and Figure 40. The performance of scenario 4 is the best of both worlds improving the target curve across its entire range. The NPV Value at Risk is in positive territory improving by 135% from -$757M → $268M. The NPV Value at Gain P95 improved 35% from $4.2B to $5.7B. The overall NPV average improved by 46% from $1.6B to $2.3B. These figures confirm that the flexibility is complementary and there does not appear to be a downside to their combination in this situation.

KPI	S0: Static Base Case	S1: Base Case with Uncertanty	S1 vs S0	S2: Uncertanty Model with Scaling Flexibility	S2 vs S1	S3: Baseline with SPC Flexibility	S3 vs S1	S4: Baseline with Scaling and SPC Flexibility	S4 vs S1
NPV (mean)	$2346 M	$1562 M	-33%	$1814 M	16%	$1932 M	24%	$2276 M	46%
NPV (std dev)		$1635 M		$1975 M	21%	$1281 M	-22%	$1747 M	7%
NPV Min		-$7292 M		-$5233 M	-28%	-$905 M	-88%	-$456 M	-94%
NPV Max		$7613 M		$13160 M	73%	$6800 M	-11%	$11107 M	46%
Value At Risk, P5, $		-$757 M		-$396 M	-48%	$135 M	-118%	$268 M	-135%
Value At Risk, P10, $		-$144 M		-$43 M	-70%	$393 M	-372%	$510 M	-454%
Value at Gain, P90, $		$3620 M		$4366 M	21%	$3681 M	2%	$4614 M	27%
Value at Gain, P95, $		$4245 M		$5523 M	30%	$4244 M	0%	$5743 M	35%

Figure 38 Scenario 4: Statistical KPI Comparison

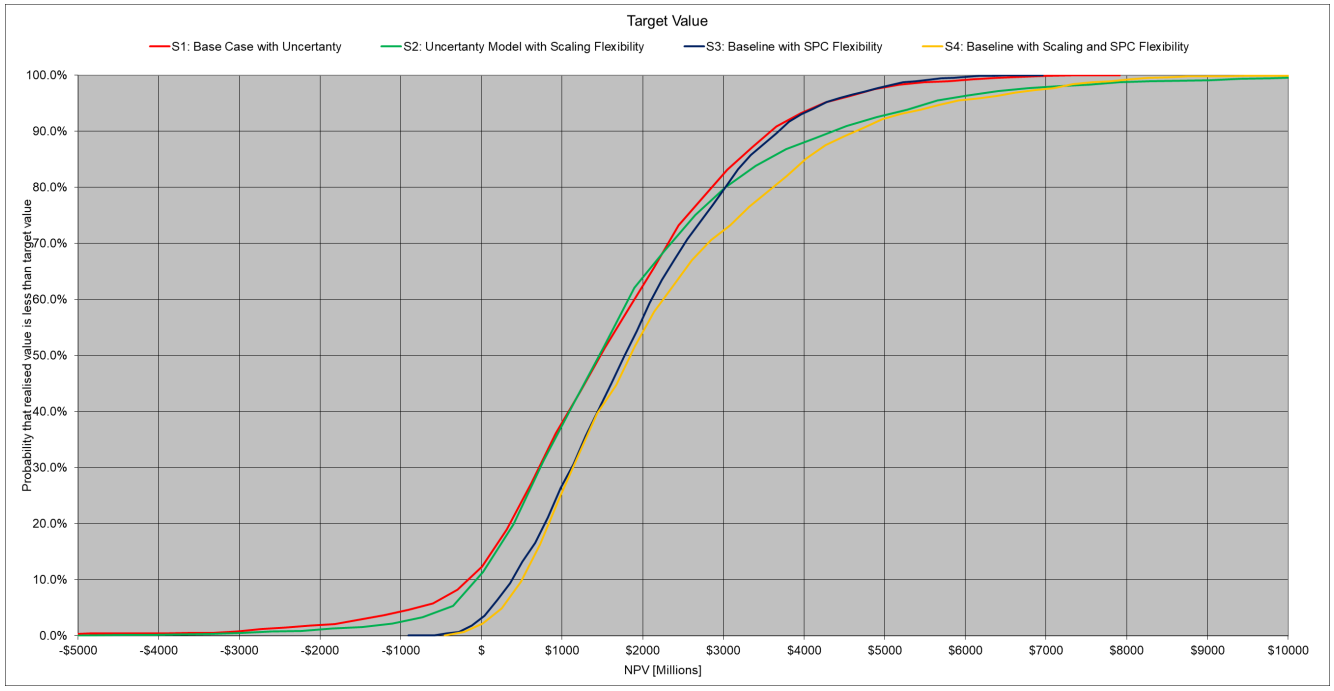


Figure 39 Scenario 4: Target Value Comparison

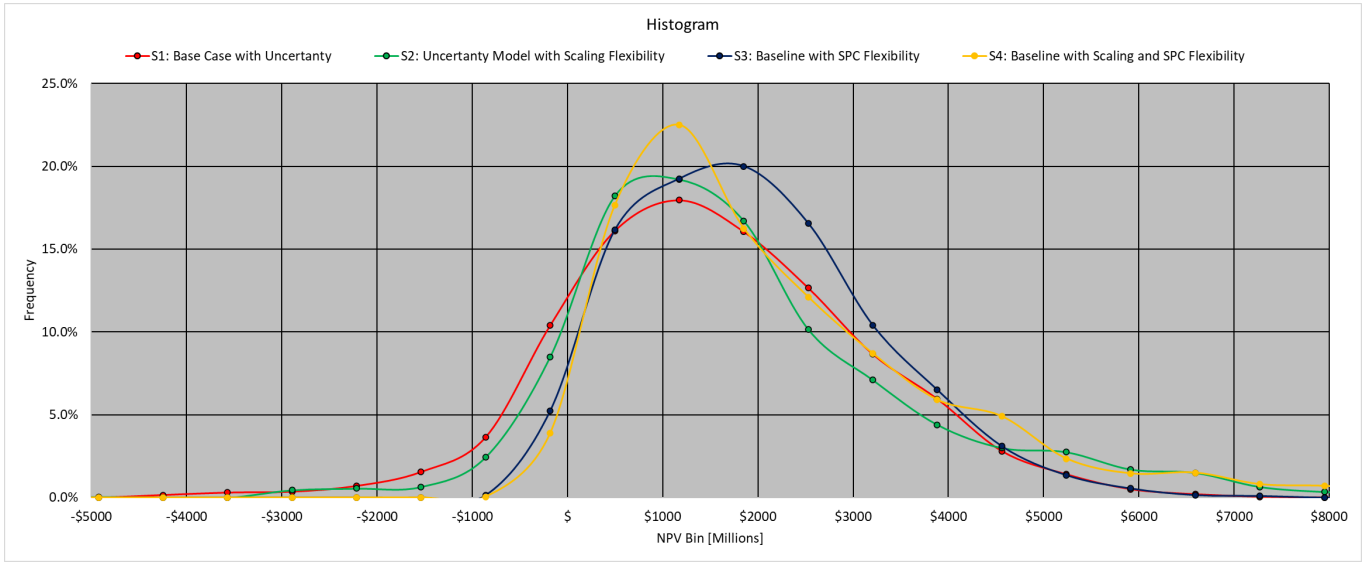


Figure 40 Scenario 4: Histogram Comparison

Scenario Recommendation

Based on the data generated by the Monte Carlo simulations, Scenario 4, which includes both scaling flexibility and SPC flexibility is the recommended approach. It dominates all aspects of the target curve and has no compromises. It would be the clear recommendation going forward.
This scenario minimizes the overall value at risk by 135% and significantly improves the value at gain by 35% and increases the overall NPV average by 46%. Overall, this scenario confirms the viability of this investment as it demonstrates a significantly positive NPV across a wide range of probable outcomes which can be translated as long-term viability and success of this new pacemaker technology in a dynamic and uncertain future.

Lessons Learned

What you learned through the process of doing the application?

Two significant insights emerged from doing this exercise which influenced my overall understanding.

First, my original assumptions about what sources of uncertainty would have the biggest impact were wrong. I had originally assumed the R&D expenses and FDA Timing would be the biggest drivers of variation in the NPV. I assumed this because of my personal biases working closely to those areas. It was when we created the tornado diagrams for the sensitivity analysis that the underlying relationships were uncovered. This type of sensitivity analysis is something I'm going to bring to other areas of my work.

Second was internalizing that there is no one correct answer but always a distribution of answers. Learning that we need to look through how our decisions and optimizations have impact on the shape of distribution not just on a single static "average" case.

Where you see the most use for the Flexible approach to design?

I believe flexible design can be used at many different levels of abstraction. I can image scenarios where it could be used in organization management, complex program planning, or even focusing on the lifecycle planning of a low-level component. As we many things, it's going to have the biggest impact where significant time, money, and resources are involved.

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