Using Mixed-Methods Development-Focused HTA and NPV Calculations to Guide Further Investment and R&D:

A Value Proposition for Biosensor-Integrated Arteriovenous Grafts

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Background & Objectives

- Assessing the potential clinical and economic value of medical devices under development is necessary to guide further research and investment decisions, yet such assessments remain challenging.

- ***This study illustrates the utility of a mixed methods approach, including qualitative methods, decision-analytic modelling, and risk-adjusted net present value (rNPV) analysis, in exploring the value of an example technology; a biosensor-integrated self-reporting arteriovenous graft (subsequently referred to as smart AVG).***

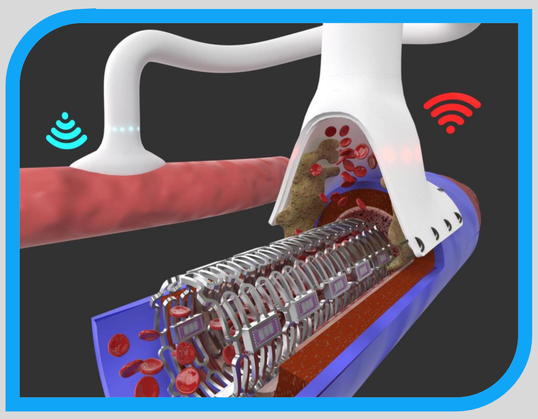

Fig. 1: A 3D illustration of the Smart AVG

- The arteriovenous graft (AVG) is one of the main options for hemodialysis vascular access.
- Current grafts have high rates of stenosis, i.e. narrowing of the graft lumen, leading to poor functionality.
- Currently in preclinical development, the smart AVG will use impedance spectroscopy to detect stenosis *(surveillance use case)* and electrically induce apoptosis to treat stenosis (*interventional use case*). Both functions have only been demonstrated in-vitro[1-3] but the clinical value proposition is yet to be established.

Methods

1. Qualitative Clinician Stakeholder Engagement

- A stakeholder engagement was conducted with US and UK clinicians including interventional cardiologists, a peripheral endovascular specialist, an interventional nephrologist and a vascular surgeon.
- Clinicians expressed their views on if and how the technology may alter clinical pathways in the wake of arteriovenous graft stenoses.

2. Decision Analytic Modelling

- Cost-utility analysis (decision tree and Markov model)
- Compared the smart AVG with currently used AVGs (expanded polytetrafluoroethylene (ePTFE) grafts)
- Analysis estimated the incremental net monetary benefit (INMB) of the smart AVG over the ePTFE graft for assumed levels of smart AVG effectiveness.
- A US Medicare perspective was used over a 62-month horizon.
- Model parameters were derived from relevant literature.

3. Risk-adjusted Net Present Value (rNPV) Analysis

- Using the INMB as the unit cost of the smart AVG, the rNPV and hence the commercial viability of the device was estimated over an assumed developmental lifespan (12 years) up to 10 years of sales.
- rNPV = *Discounted future cash inflow – Discounted future cash outflow.*
- Cash flows were adjusted by the probability of success at the end of each developmental stage.
- The average cost, duration and probability of success of development of Class III FDA devices were used. [4,5]

Results

- Stakeholder engagement revealed difficulty in establishing the current value of the surveillance use case due to the lack of well-established and effective interventions for preclinical stenosis, i.e., stenosis without clinical signs.
- Based on this, the cost-utility analysis focused on the interventional use case and estimated economically justifiable prices at assumed levels of effectiveness.
- Using these prices, rNPVs were estimated in the final stage.

Table 1. An example of rNPV calculation for an assumed level of effectiveness of the smart AVG for an interventional use case.

	Item	Estimate
	Target Weighted average cost of capital	10.4%
	Assumed smart AVG effectiveness	60%
Revenues	Unit Price	$22,832
	Unit Cost of Goods	$100
	S & G Costs as a percentage of Sales Revenue	30%
	Total Forecast Unit Sales 2035-2044	130,368
	Net revenue if successful	$2,070,523,018
	Overall Probability of Success	13.7%
	Probability Success Weighted Net Revenue	$284,652,009
	Discount Factor for Future Sales	81.6%
	Discounted Total Revenue	$52,477,862
Cost of Development	Probability Weighted Development Costs	$48,768,344
	Discount Factor for Future Development Costs	31.5%
	Discounted Total Costs	$33,412,169
Risk-adjusted NPV		**$19,065,693**

Smart AVG effectiveness was expressed as percentage reductions in graft failure from stenosis when compared to ePTFE grafts. Unit price was the INMB estimated from the cost-utility analysis using a willingness-to-pay threshold of $100,000 per QALY. The cost of goods was assumed as the additional manufacturing cost of the smart AVG over that of the ePTFE graft.

Table 2. Two-way sensitivity table showing rNPV as smart AVG effectiveness and cumulative probability of developmental success are varied

Cumulative probability of success \ Effectiveness of Smart AVG	*0%*	*20%*	*30%*	*41%*	*50%*	*60%*	*80%*
0.0%	-$12,277,791	-$12,277,791	-$12,277,791	-$12,277,791	-$12,277,791	-$12,277,791	-$12,277,791
5.0%	-$27,051,297	-$21,349,591	-$18,255,090	-$14,644,392	-$11,516,962	-$7,845,256	$183,407
10.0%	-$31,211,533	-$19,808,121	-$13,619,119	-$6,397,723	-$142,863	$7,200,550	$23,257,874
13.7%	**-$33,742,589**	**-$18,065,371**	**-$9,556,836**	**$371,018**	**$8,970,093**	**$19,065,693**	**$41,141,032**
20.0%	-$37,413,498	-$14,606,675	-$2,228,671	$12,214,121	$24,723,840	$39,410,666	$71,525,316
25.0%	-$40,039,990	-$11,531,460	$3,941,045	$21,994,534	$37,631,683	$55,990,216	$96,133,528
30.0%	-$42,481,010	-$8,270,774	$10,296,231	$31,960,419	$50,724,998	$72,755,237	$120,927,211
35.0%	-$44,782,310	-$4,870,369	$16,791,138	$42,066,024	$63,958,032	$89,659,977	$145,860,614
40.0%	-$46,973,332	-$1,359,685	$23,396,323	$52,281,907	$77,301,345	$106,674,997	$170,904,296
45.0%	-$49,074,340	$2,241,013	$30,091,521	$62,587,803	$90,734,671	$123,780,030	$196,037,991
50.0%	-$51,099,995	$5,917,064	$36,862,074	$72,969,054	$104,243,351	$140,960,416	$221,247,040

A two-way sensitivity analysis was conducted for varying levels of smart AVG effectiveness and varying cumulative probability of developmental success. Using the average cumulative probability of success for the development of a Class III device (13.7%) as cited by Sertkaya et al.[4] a minimum effectiveness level of 41% was necessary for a cost-effective smart AVG that yields a positive rNPV.

Conclusion

This multi-stage approach assesses the value of a new technology by identifying under which conditions (such as clinical study success, appropriate discount rates, potential market size and product penetration, and assumptions associated with cost-effectiveness modelling and reimbursement) investment in R&D may be regarded as commercially attractive.

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