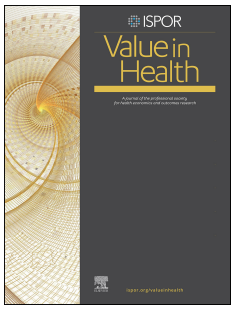

Central venous access devices for the delivery of systemic anticancer therapy: an economic evaluation

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Highlights

- Several clinical trials have demonstrated that PORT is associated with fewer complications, compared with HICK or PICC devices. A recent study found that the total cost of PORT was greater than PICC and similar to HICK. However, accounting for catheter dwell time, the cost per catheter week was lower for PORT. While there was no meaningful difference in QALYs gained using PORT, several qualitative studies have suggested a preference for PORT among patients.
- Cost-effectiveness in the UK is typically assessed using the cost-per-QALY framework. However, in the context of a complex intervention, such as a medical device, the cost-per-QALY framework is not always appropriate. This is because complex interventions may impact on a range of outcomes relevant to patients and decision-makers. Furthermore, when considering complex interventions, implementation is key – that is, where and how an intervention will be implemented in routine practice.
- In this study a cost-consequence analysis was employed to disaggregate a range of clinical and economic outcomes associated with the choice of venous access device. We found that PORT is superior to both HICK and PICC, for the majority of outcomes we measured – most importantly, for safety and cost. In addition, a Value of Implementation analysis found that PORT was likely to be considered cost-effective in routine practice within the NHS.

Abstract

Objectives: Patients undergoing long-term anti-cancer therapy typically require one of three venous access devices (VADs): HICK, PICC, or PORT. Recent evidence has shown PORT is safer and improves patient satisfaction. However, PORT did not show improvement in quality-adjusted life years (QALYs) and was more expensive. Decisions regarding cost-effectiveness in the UK are typically informed by a cost-per-QALY metric. However, this approach is limited in its ability to capture the full range of relevant outcomes, especially in the context of medical devices. This study assessed the potential cost-effectiveness of HICK, PICC and PORT in routine clinical practice.

Methods: Cost-consequence analysis to determine the trade-offs between the following outcomes: complication, infection, non-infection, chemotherapy interruption, unplanned device removals, health utilities, device insertion cost, follow-up cost, and total cost, using data from the CAVA clinical trial. We conducted Value of Implementation analysis of a PORT service.

Results: PORT was superior in terms of overall complication rate, compared with both HICK (IRR: 0.422 (95% CI: 0.286 to 0.622)) and PICC (IRR: 0.295 (95% CI: 0.189 to 0.458)) and less likely to lead to an unplanned device removal. There was no difference in chemotherapy interruption or health utilities. Total cost with device in situ was lower on PORT, compared with HICK (£-98.86 (95% CI: -189.20 to -8.53)) and comparable with PICC -£48.57 (95% CI: -164.99 to 67.86)). Value of Implementation analysis found that PORT was likely to be considered cost-effective within the NHS.

Conclusion: Decision makers should consider including PORT within the suite of VADs available within in the NHS.

Highlights

- Several clinical trials have demonstrated that PORT is associated with fewer complications, compared with HICK or PICC devices. A recent study found that the total cost of PORT was greater than PICC and similar to HICK. However, accounting for catheter dwell time, the cost per catheter week was lower for PORT. While there was no meaningful difference in QALYs gained using PORT, several qualitative studies have suggested a preference for PORT among patients.
- Cost-effectiveness in the UK is typically assessed using the cost-per-QALY framework. However, in the context of a complex intervention, such as a medical device, the cost-per-QALY framework is not always appropriate. This is because complex interventions may impact on a range of outcomes relevant to patients and decision-makers. Furthermore, when considering complex interventions, implementation is key – that is, where and how an intervention will be implemented in routine practice.
- In this study a cost-consequence analysis was employed to disaggregate a range of clinical and economic outcomes associated with the choice of venous access device. We found that PORT is superior to both HICK and PICC, for the majority of outcomes we measured – most importantly, for safety and cost. In addition, a Value of Implementation analysis found that PORT was likely to be considered cost-effective in routine practice within the NHS.

Introduction

Patients who undergo long-term anti-cancer therapy typically require one of three venous access devices (VADs): subcutaneously tunnelled central catheters (Hickman-type device; HICK), peripheral inserted central catheters (PICC) or implantable chest wall port (PORT) [1]. HICK has traditionally been the most commonly used device. However, the ease of insertion and perception that HICK and PICC were comparable in terms of safety, meant that the use of PICC has come to dominate in recent years [2]. While PORT has been available for several decades, a lack of evidence on the cost-effectiveness of PORT and how such a service would be delivered, are possible reasons why the use of PORT has remained minimal in the UK.

Previous research found that PORT was associated with fewer complications compared with both HICK [3] and PICC [4]. Despite the greater initial insertion cost associated with a PORT, the reduced rate of complications led to a lower cost compared with HICK [5] and PICC devices [6]. However, another study found no difference in cost, despite the lower rate of complications on a PORT [7]. Most recently, the Cancer and Venous Access (CAVA) trial found that HICK and PICC were comparable in terms of overall complications, and that PORT was superior to both HICK (OR 0·54 (95% CI: 0·37–0·77)) and PICC (OR 0·52 (95% CI:0·33–0·83)) [8]. A cost-utility analysis alongside the CAVA trial compared the costs and quality-adjusted life-years (QALYs) associated with the use of each device [9]. PORT was associated with a small, non-statistically significant, difference in cost (-£45) and QALYs (0.004) compared with HICK and a large difference in cost (£1,665), but small, non-statistically significant, difference in QALYs (-0.018) compared with PICC.

Qualitative research suggests that PORT is associated with benefits not captured within the QALY metric [7,9,10]. Using a device-specific questionnaire, Patel, et al (2014) found that while there was no measured difference in quality of life between PORT and PICC, patients

reported that there were aspects of quality of life not captured within the study's questionnaire - in particular, the ability to shower, bath and swim while using a PORT [7]. A significant benefit in favour of PORT was observed using a device-specific questionnaire in the CAVA study, which focused on questions relating to daily activities (e.g. mobility, exercise, ability to work, appearance) [9]. A qualitative analysis involving 42 patients over eight focus groups identified a pattern of device preferences that favoured PORT [10]. In particular, PORT was perceived to offer unique psychological benefits, including a greater sense of freedom and the ability to "forget" about their treatment.

Decisions regarding the cost-effectiveness of health technologies in the UK are typically informed by a cost-utility (cost-per-QALY) analysis, as recommended by the National Institute for Health and Care Excellence (NICE) guidance for technology appraisal. Because QALYs are not disease specific, the cost-per-QALY approach can be used to compare the net benefit of a health technology across diseases areas. This makes the cost-per-QALY framework extremely valuable for decision making. However, this approach is not always sufficient for the evaluation of complex interventions, such as medical devices. This is because the introduction of a complex intervention may impact on a range of clinical and economic outcomes which are not captured within the cost-per-QALY framework. Given the challenge of capturing the impact of a VAD within the cost-per QALY framework, previous findings on the relative cost-effectiveness of HICK, PICC or PORT may have been limited. In the context of oncology, the quality of life of patients receiving anti-cancer therapy may be dominated by the disease burden associated with cancer and chemotherapy. As a result, benefits associated with a VAD may be overlooked. Furthermore, there is currently a lack of clarity in terms of how VADs should be delivered in routine practice [11]. HICK and PORT are typically delivered in a theatre setting, whereas PICC can be delivered at the bedside (personal communication, The Beatson, Glasgow). Therefore, limited access to a theatre

setting means that the use of PICC may be based on necessity rather than evidence-based practice. The aim of this study was to estimate the cost-effectiveness of HICK, PICC and PORT devices in routine clinical practice in the UK, using data from the CAVA trial.

Methods

We undertook an economic evaluation, using a cost-consequence approach, to determine the trade-offs between a range of clinical and economic outcomes that are relevant to patients and decision makers. Methods were reported in line with the CHEERS checklist for economic evaluation [12]. We used data from the CAVA trial that compared the clinical effectiveness of HICK, PICC and PORT [8]. An individual participant (IPD) network meta-analysis (NMA) was used to estimate clinical and economic outcomes from the four randomisation options of the CAVA trial. In addition, we used a Value of Implementation analysis to estimate the cost-effectiveness of introducing a PORT service into routine clinical practice, based on a plausible implementation strategy.

Perspective, discount rate and time horizon

The cost-consequence analysis [13] was undertaken from the perspective of the UK National Health Service (NHS) over a one-year time horizon [14]. The analysis was based on the intention-to-treat population (1,061 patients) from the CAVA trial. The Value of Implementation analysis evaluated the costs and benefits associated with the implementation of a PORT service over a five-year time-period. We assumed that 1,000 patients would require a VAD at a single oncology site per year. This equates to an "effective population" (discounted population) of 4,673 patients over five years [15,16]. The population was discounted at 3.5%.

Clinical and economic outcomes

We estimated nine outcomes of interest to patients and decision makers which were available from the CAVA trial – six clinical outcomes and three economic outcomes (Table 1). The trial captured resource use relating to device insertion and follow-up visits. The resource use associated with device insertion included both staff and setting requirements, alongside the cost of the VAD itself. Follow-up visits included both unplanned inpatient and outpatient visits occurring during the follow-up period as a result of a device-related complication. Unit costs were attached to all resource use items and costs were presented for the price year 2017/18. Staff, setting and device specific unit costs were used to estimate device-insertion costs. A unit cost which represents the average resource utilisation for an inpatient stay, and outpatient visit, respectively, was used. Full details of the clinical and economic outcomes and methodology is available elsewhere [9].

INSERT TABLE 1

Individual patient data network meta-analysis

The CAVA trial recruited participants via four randomisation options. Therefore, each randomisation option was treated as a separate sub-study in the analysis. We used a two-stage multivariate random effects model to perform the individual participant data network meta-analysis [17]. In the first stage, we used the individual participant data to estimate summary measures for each study for each outcome of interest. Final estimates combined in NMA were based on the difference in effect between a device and a reference device (HICK).

The difference in the log mean rate for all count outcomes (complication, infection, non-infection complication, number of days of chemotherapy interruption) was estimated using a negative binomial regression, accounting for the time with device in situ for each patient. Results were exponentiated and presented as the incidence rate ratio (IRR).

To estimate the odds of an unplanned device removal we created two groups – planned device removal and unplanned device removal – based on the reasons for device removal data obtained from the CAVA trial. Within the planned removal group were the following reasons: planned removal/end of treatment, and patient deceased. Within the unplanned device removal were the following reasons: removal for complications, removal due to patient preference, removal for other reason. We used logistic regression to estimate the odds of being in the unplanned device removal group, based on device received. A full breakdown of the number of patients in each group in given is Supplementary Material.

The difference in mean health utilities was estimated using a mixed-effects linear regression, accounting for the repeated measure of patients' health utility over the trial period.

The mean device insertion cost for each device was estimated using a generalised linear model (GLM). Follow-up costs per catheter week consisted of inpatient and outpatient costs

during the follow-up period, divided by the dwell time (in weeks) on device. As there were patients with no follow-up costs, we used a logit regression to estimate the proportion of patients with zero costs, and GLM with log link and gamma family to estimate mean follow-up costs, conditional on the patient having a positive follow-up cost. The mean total patient cost (combination of device insertion and follow-up cost) per catheter week over the trial period was estimate using a GLM, with log link and gamma family.

We adjusted our regression models for the trial stratification factors: body mass index (BMI), device history, site of enrolment [18]. The stratification factors were defined as follows: BMI was dichotomised into $<30mg/kg^2$ and $\geq 30mg/kg^2$; device history was categorised as "any history" or "no history", and site of enrolment retained the six sites with the highest recruitment and combined the smaller sites into one "other" site.

The results of the NMA are presented as a cost-consequence analysis (Table 3). We used a "traffic light system" to demonstrate where a device was statistically significantly superior (green) to the reference device, no different (amber), or statistically significantly inferior (red). We also ranked each device according to the surface under the cumulative ranking (SUCRA) curve method for each outcome of interest [19].

Value of Implementation analysis

We used the Value of Implementation framework to estimate the value to the NHS of implementing PORT into routine practice [20]. This approach involves using an estimate of the net benefit – expressed as the value of reducing complications in monetary terms. We estimated the net benefit for a typical individual, then scaled this up to the eligible population to estimate the population net benefit and subtracted from this the cost of implementation. If the population net benefit was greater than the cost of implementation, then implementation was considered cost-effective.

To determine the Value of Implementation in routine clinical practice, we needed to incorporate additional costs which were not captured within the CAVA trial. Based on expert opinion (interviews with clinicians at The Beatson Institute for Cancer Research and The Christie NHS Foundation Trust), we developed a plausible scenario for the delivery of a PORT service. In our scenario, we assume 1,000 patients would require a venous access device at a single oncology site per year. Based on consultation with clinical experts, we assume a base case in which 50% of patients requiring a VAD receive a PORT. While on treatment, patients would require regular device maintenance (e.g. flushing) [1], device replacement if necessary, and device removal at treatment completion. In the first year of implementation, staff would incur additional training costs. Full details of the assumptions made in the base case analysis and uncertainty analysis are given in Supplementary Material.

We used the expected difference in the number of complications per patient on a PORT, compared with a HICK or PICC, alongside costs, to estimate the potential cost-effectiveness of the implementation of PORT. To monetise the expected net benefit of a PORT, we attached a willingness to pay of £20,000 per complication avoided. This value is commonly used to assess cost-effectiveness in the UK, based on a WTP for QALY gains. While a range

of methods exist to value health gains [21], there is no commonly accepted WTP for avoiding complications in this patient population. However, the avoidance of inconvenient and potentially dangerous complications represent a clear benefit to patients. Furthermore, previous qualitative research highlighted the value of PORT in terms of comfort and ability to perform daily tasks. Therefore, while limited in this context, the WTP value of £20,000 is used to give an indication of potential cost-effectiveness. The minimum potential WTP value for complications avoided is tested in sensitivity analysis. We undertook the following base case and sensitivity analyses relating to implementation of a PORT service:

Base case: What is the value of achieving 50% implementation (base case)?

Sensitivity analysis 1: What is the value of full implementation (100% of patients receiving PORT)?

Sensitivity analysis 2: What level of implementation do we require for the benefits to exceed the cost?

Sensitivity analysis 3: What is the maximum implementation cost allowable for benefits to exceed costs?

Sensitivity analysis 4: What is the minimum willingness to pay threshold for complications avoided that would be required for PORT to be cost-effective in practice?

INSERT TABLE 2

Parameter values in Table 2 were used in the following Value of Implementation equation:

$N(\sigma-\rho) * ((WTP*\Delta Q) - \Delta C1) - C2 > 0$

Where:

N = patient population, σ = utilisation following implementation activity, ρ = current level of utilisation, WTP = willingness to pay for complications avoided, Q = number of complications avoided, C1 = cost per procedure, C2 = implementation cost.

Results

Results of individual participant data network meta-analysis

PORT was ranked as the best choice of device for seven out of the nine outcomes measured in this analysis (Table 3). PICC was ranked best for two outcomes – device insertion cost and health utilities. However, the magnitude of effect and confidence intervals shows that there was little difference in health utilities among devices. HICK did not rank best for any outcomes.

In terms of the rate of overall complications, PORT was superior to both HICK and PICC. This was primarily driven by the benefit of PORT in relation to non-infection complications. While PORT was superior to HICK in terms of infection rate, there was no significant difference in infection rate between PORT and PICC.

PORT was superior to both HICK and PICC in terms of the odds of an unplanned device removal. There was no meaningful difference among devices for both days of chemotherapy interruption and follow-up costs.

While the initial device insertion was more expensive for PORT compared with either HICK or PICC, the total cost with device in situ was significantly less on PORT, compared with HICK and comparable with PICC.

INSERT TABLE 3

Value of Implementation

The value to the NHS of PORT being receiving by 50% of eligible patients is approximately £13m compared with HICK, and £8m compared with PICC. That is, the benefit of PORT, in terms of the monetary value we place on avoiding complications, is greater than the cost of implementing a PORT service. If PORT is received by 100% of eligible patients, the Value of Implementation is £25.5m compared with HICK, and £16.2 compared with PICC.

Any level of implementation (greater than zero) of a PORT service is likely to be cost-effective, compared with both HICK and PICC. This is due to the value of the complications avoided, compared with the implementation (set-up) costs and per patient treatment cost.

The maximum cost of implementation for which PORT would still be considered cost-effective is £12m compared with HICK, and £8m compared with PICC.

At a level of £0 willingness to pay for complications avoided, the value of PORT implementation is £2.5m compared with HICK. The minimum level of WTP for PORT to be considered cost-effective, compared with PICC, is £1,600. That is, if we are willing to pay at least £1,600 to avoid a complication, PORT is cost-effective compared with PICC.

Our Value of Implementation analysis suggests that PORT, compared with HICK or PICC, is likely to be considered a cost-effective use of resources based on a range of sensitivity analyses (Table 4). An additional sensitivity analysis, based on infections avoided and the WTP to avoid infections, is provided in Supplementary Material, Table 5.

INSERT TABLE 4

Discussion

Our cost-consequence analysis found that PORT was superior to both HICK and PICC for the majority of our outcomes of interest. While PORT was more costly to insert, when time on device was taken into account, the mean total cost of a PORT was lower than that of a HICK and comparable with PICC. Using the Value of Implementation framework, we have shown that the introduction of a PORT service is likely to be considered cost-effective, compared with either a HICK or PICC service, in routine clinical practice.

Cost-effectiveness, expressed as the incremental cost-per-QALY gained, is one of the most important factors for decision makers considering implementing a health technology in the UK. A previous analysis of the CAVA trial, based on a cost-per-QALY approach, found that there was significant uncertainty regarding the cost-effectiveness of PORT – driven by a lack of difference in QALY gain between devices [9]. However, there is currently little consensus on exactly when and how best to measure quality of life in oncology trials [22]. Health-related quality of life questionnaires administered before or after chemotherapy sessions may not capture important quality of life fluctuations during sessions. In the CAVA trial, preferences for a VAD may have been dominated by chemotherapy-related toxicity. Although not captured by the EQ-5D questionnaire in the CAVA trial, the avoidance of inconvenient and potentially dangerous complications represents a clear benefit to patients. Cost-consequence analysis allows the inclusion of a range of relevant outcomes, beyond the QALY, to assess the value of a technology. However, cost-consequence analysis is itself not without its limitations. In particular, where the QALY is not included as an outcome, comparison across disease areas is limited.

The Medical Research Council (MRC) recently recommended that implementation should be considered alongside economic evaluation when evaluating a complex intervention [23].

However, there is currently no clear guidance on how implementation should be incorporated within economic evaluation. In this study, the use of a cost-consequence analysis, alongside a Value of Implementation analysis, allowed us to build on the previous economic evaluation of PORT and to enhance the evidence base by considering both a wider range of outcomes which are relevant to both patients and decision makers and also how a PORT service would be implemented in routine practice.

The original analysis of the CAVA trial found that patients on a PORT were approximately half as likely to experience a complication, compared with a HICK or PICC [8]. Using both direct and indirect evidence, and adjusting our analysis for catheter dwell time, we found that patients were over twice as likely to avoid a complication on a PORT, compared with a HICK, and over three times as likely to avoid a complication compared with a PICC.

The CAVA trial found that the total cost of PORT, including device insertion and follow-up cost, was greater than HICK and PICC. However, when adjusted for catheter time in situ, PORT was less expensive that HICK or PICC. This study also found total cost, adjusted for catheter time in situ, was lower for PORT, compared with HICK or PICC. This aligns with the findings of Taxbro, et al (2019) [6] which found that PORT were 34 euros less costly, per catheter day, compared with a PICC. Two other studies also found a lower cost associated with PORT, compared with HICK [3,5]. However, in contrast with these three studies, the lower cost of PORT was not due to a reduction in complication cost. The CAVA trial found that PORT was more costly for device insertion, follow-up costs and total costs. It was only when device dwell time was taken into account that PORT was less costly. In the CAVA trial, inpatient and outpatient attendances (during follow-up) were to be recorded only if they were a result of device-related complications. Discussions with clinicians following the trial highlighted uncertainty as to whether or not this practice had been strictly followed. For

example, one patient in the PICC group subsequently spent 56 days in hospital. Clinicians in the CAVA trial suggested this was very unlikely to be related to the use of the PICC. It is possible that the cost of complications associated with a PORT may be underestimated in this study.

The Value of Implementation approach typically uses the expected mean cost difference and QALY gain for a patient as a measure of the "effect" from using the technology and compares this with the cost of setting-up and delivering this technology. However, as we have highlighted, the cost-per-QALY approach is not always suitable for the evaluation of medical devices. For this reason, we included complications avoided, as our measure of effect for the technology. We used £20,000 as our willingness to pay to avoid complications, as this is the threshold commonly used to assess cost-effectiveness in the UK. While this threshold is not designed to value complications avoided, our sensitivity analysis found that for WTP thresholds considerably lower than this (£0 compared with HICK, and £1,600 compared with PICC), PORT was likely to be considered a cost-effective use of resources. Further sensitivity analysis found that, if we focus the Value of Implementation analysis on infection as our measure of effect (rather than overall complications), the cost of implementing a PORT service was offset by the cost saving associated with the reduction in hospital admission costs due to infection. However, we acknowledge that the lack of a validated WTP to avoid complications is a limitation of this study. In addition, a limitation of the Value of Implementation framework more generally is that it still requires the focus of effect to be on a single outcome, whereas multiple outcomes are relevant to patients and decision makers in this context. A limitation shared with the cost-per-QALY approach.

In common practice, patients requiring a venous access device for planned length of treatment greater than six months are considered a PORT (personal communication, The

Beatson, Glasgow). Our results suggest that PORT is superior (more effective, less costly) compared with HICK and cost-effective (more effective, similar cost) compared with PICC for patients requiring long-term (≥12 weeks) anti-cancer therapy for solid malignancy. PORT should therefore be considered, alongside PICC, as a safe and cost-effective device option for this patient population. While the benefits of PORT, particularly relating to clinical outcomes, are likely to be generalisable across settings, the costs associated with the delivery of PORT are likely to be context specific.

A future challenge is to configure service delivery such that PORT insertion and removal services become more widely available and able to provide a timely and cost-effective service. A nurse-led service, in line with what is currently provided at The Christie NHS Foundation Trust, where a PORT is inserted by one or two trained nurses in a basic procedure room, would be one way to achieve this. Oncology nurses will require the skills and confidence to utilise these devices appropriately. Alternatively, it may mean grouping procedures into sessions where adequately trained staff (doctors, surgeons, radiologists, and nurses) can process procedures quickly and safely. With ultrasound, ECG catheter guidance and other advances, such procedures may no longer need to be performed in expensive theatre or angio suite environments.

The CAVA trial found that, despite having an overall lower number of complications, PORT was associated with a greater number of infections compared with PICC [8]. Taxbro et al (2019) found similar findings [4]. However, both CAVA and Taxbro reported that when adjusted for device dwell time PORT had a lower infection rate than PICC in both trials. Further research into the cause of PORT-related infection, and how this can be minimised through improved insertion and removal techniques is warranted. Due to the small number of

haematological cancer patients in the CAVA trial, the clinical and cost-effectiveness of PORT remains unclear for patients requiring long-term anti-cancer therapy in this population.

Conclusion

In this study we have shown how the use of cost-consequence analysis can overcome the limitations of the cost-utility framework in the evaluation of complex interventions. Our findings suggest that PORT is both safer and, when catheter dwell time is taken into account, comparable in terms of cost. PORT is therefore likely to be cost-effective use of NHS resources. Decision makers should consider introducing PORT into the suite of venous access device options available for patients in the UK NHS.

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Table 1: Summary measures included, definition, data format, estimation procedure, and summary statistic obtained

	Definition	Data format	Estimation procedure	Summary statistic
Clinical outcomes				
Complication	Composite of infection (suspected or confirmed) or mechanical failure	Count	Negative binomial regression	Incidence rate ratio (IRR)
Infection	Composite of laboratory-confirmed blood stream infection, possible catheter-related blood stream infection, exit site infection.	Count	Negative binomial regression	Incidence rate ratio (IRR)
Non-infection complication	Composite of inability to aspirate blood, venous thrombosis related to device, pulmonary embolus related to device, mechanical failure, other complications.	Count	Negative binomial regression	Incidence rate ratio (IRR)
Days of chemotherapy interruption	Number of days of chemotherapy interruption during the trial period.	Count	Negative binomial regression	Incidence rate ratio (IRR)
Unplanned device removal	Device removal due to complications, patient preference, or other reasons.	Binary (yes/no)	Logistic regression	Difference in odds ratio
Health utilities	Health related quality of life measured using the EQ-5D-3L questionnaire.	Continuous	Mixed-effects regression	Difference in mean
Costs				
Device insertion cost	Cost of device and cost of staff and setting required for insertion.	Continuous	GLM regression	Difference in mean (total)
Follow-up costs (Inpatient + outpatient) per catheter week	Unplanned inpatient and outpatient visits during the follow-up period.	Continuous	Two-part model (logit and GLM)	Difference in mean (per catheter week)
Total cost per catheter week	Device insertion cost plus follow-up costs.	Continuous	GLM regression	Difference in mean (per catheter week)

Table 2: Base case parameter values for value of implementation analysis

Inputs	HICK	PICC
Number of patients eligible for VAD at single oncology centre over 5 years	5,000	5,000
Effective (discounted) population	4,673	4,673
Currently level of utilisation of PORT, compared with HICK and PICC)	0%	0%
Utilisation following implementation activity	50%	50%
Willingness to pay for complications avoided	£20,000	£20,000
Difference in number of complications avoided (compared with PORT)	0.21	0.18
Difference in procedure cost (compared with PORT)	£-937	£268
Difference in cost of implementation over 5 years (compared with PORT)	£2,557	£5,602

Table 3: Results of network meta-analysis for each outcome of interest

	Surface under the cumulative ranking curve (SUCRA)	PICC V HICK*	PORT V HICK*	PORT V PICC*
Complication rate (IRR)	Best: PORT Worst: PICC	1.433 (0.234, 1.973)	0.422 (0.286, 0.622)	0.295 (0.189, 0.458)
Infection complication rate (IRR)	Best: PORT Worst: HICK	0.412 (0.258, 0.661)	0.307 (0.199, 0.473)	0.744 (0.419, 1.320)
Non-infection complication rate (IRR)	Best: PORT Worst: PICC	2.590 (1.425, 4.706)	0.510 (0.271, 0.958)	0.197 (0.103, 0.378)
Days of chemotherapy interruption (IRR)	Best: PORT Worst: HICK	0.262 (0.056, 1.225)	0.212 (0.042, 1.062)	0.809 (0.154, 4.256)
Unplanned device removal (difference in odds ratio)	Best: PORT Worst: HICK	1.076 (0.988, 1.171)	0.828 (0.767, 0.893)	0.769 (0.702, 0.843)
Health utilities (difference in mean)	Best: PICC Worst: PORT	0.006 (-0.021, 0.033)	-0.007 (-0.034, 0.020)	-0.013 (-0.040, 0.014)
Device insertion cost (total) (difference in mean) (£)	Best: PICC Worst: PORT	£-604.68 (-643.83, -565.54)	£368.12 (323.88, 412.36)	£972.80 (917.83, 1027.78)
Follow-up costs (inpatient + outpatient) (per catheter week) (difference in mean) (£)	Best: PORT Worst: HICK	£-55.16 (-201.33, 91.00)	£-105.14 (-242.20, 31.93)	£-49.98 (-159.28, 59.33)
Total cost (per catheter week) (difference in mean) (£)	Best: PORT Worst: HICK	£-50.30 (-181.31, 80.72)	£-98.86 (-189.20, -8.53)	£-48.57 (-164.99, 67.86)

Key – green: new device is statistically significantly better than the reference device. Amber: there is no statistically significant difference between devices. Red: new device is statistically significantly worse than the reference device. *Reference device

Table 4: Value of implementation base case results and sensitivity analysis

PORT, compared with HICK		
Sensitivity analysis	**Question**	**Result**
Base case	What is the value of 50% implementation?	£13m (95% credibility interval: £11.6m, £14m)
Sensitivity analysis 1	What is the value of full implementation (100% of patients receiving PORT)?	£25.5m (95% credibility interval: £23m, £28m).
Sensitivity analysis 2	What level of implementation is required for benefits > costs?	Threshold: any level of implementation > 0. The value of implementation at a threshold of 0.01 implementation is £250,000 (95% credibility interval: £230,000, £280,000).
Sensitivity analysis 3	What is the maximum cost of implementation allowable for benefits > costs?	Threshold: implementation cost of £12m. The value of implementation, at implementation cost of £12m, is £761,000 (95% credibility intervals: £-500,000, £2m).
Sensitivity analysis 4	What is the minimum willingness to pay (WTP) for complications avoided for benefits > costs?	Threshold: £0 WTP. The value of implementation, at implementation cost of £2,557, is £2.5m (95% credibility intervals: £1.5m, £3.5m).
PORT, compared with PICC		
Sensitivity analysis	**Outcome**	**Result**
Base case	What is the value of 50% implementation?	£8m (95% credibility interval: £7.5m, £.9m)
Sensitivity analysis 1	What is the value of full implementation (100% of patients receiving PORT)?	£16.2m (95% credibility interval: £15m, £18m).
Sensitivity analysis 2	What level of implementation is required for benefits > costs?	Threshold: any level of implementation > 0. The value of implementation at threshold of 0.01 implementation is £157,000 (95% credibility interval: £145,000, £170,000).
Sensitivity analysis 3	What is the maximum cost of implementation allowable for benefits > costs?	Threshold: implementation cost of £8m. The value of implementation, at implementation cost of £8m, is £140,000 (95% credibility intervals: £-500,000, £800,000m).
Sensitivity analysis 4	What is the minimum willingness to pay (WTP) for complications avoided for benefits > costs?	Threshold: £1,600 WTP. The value of implementation, at implementation cost of £5,602, is £30,000 (95% credibility intervals: £-250,000, £270,000).