

# Endovascular versus surgical creation of arteriovenous fistula in hemodialysis patients: Cost-effectiveness and budget impact analyses

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## Abstract

**Objectives:** The aim of the present study was to perform cost-effectiveness and budget impact analyses comparing endovascular arteriovenous fistula creation to surgical arteriovenous fistula creation in hemodialysis patients from the National Healthcare Service (NHS) perspective in Italy.

**Methods:** A systematic literature review has been conducted to retrieve complications' rates after arteriovenous fistula creation procedures. One study comparing endovascular arteriovenous fistula creation, performed with WavelinQ device, to the surgical approach through propensity score matching was preferred to single-arm investigations to execute the economic evaluations. This study was chosen to populate a Markov model to project, on a time horizon of 1 year, quality adjusted life years and costs associated with endovascular arteriovenous fistula (WavelinQ) and surgical arteriovenous fistula options for both cohorts of incident and prevalent hemodialysis patients.

**Results:** For both incident and prevalent hemodialysis patients, endovascular arteriovenous fistula creation, performed with WavelinQ, was the dominant strategy over surgical arteriovenous fistula approach, showing less cost and better patients' quality of life. Compared to the current scenario, progressively increasing utilization rates of WavelinQ over surgical arteriovenous fistula creation in the next 5 years in incident hemodialysis patients are expected to save globally 30–36 million euros to the NHS.

**Conclusion:** Endovascular arteriovenous fistula creation performed with WavelinQ could be a cost-saving strategy in comparison with the surgical approach for patients in hemodialysis. Future studies comparing different devices for endovascular arteriovenous fistula creation versus the surgical option would be needed to confirm or reject the validity of this preliminary evaluation. In the meantime, decision-makers can use these results to take decisions on the diffusion of endovascular procedures in Italy.

## Keywords

Endovascular procedure, endovascular arteriovenous fistula, WavelinQ, surgical procedure, arteriovenous fistula, hemodialysis, cost-effectiveness analysis, budget impact analysis, medical devices

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## Introduction

Globally, there are more than two million patients undergoing hemodialysis (HD) treatments.<sup>1</sup> To receive this therapy, many patients depend on a permanent vascular access.<sup>2</sup> Autogenous arteriovenous access, created by anastomosing a native artery and vein to create an arteriovenous fistula (AVF), is the preferred choice for long-term HD since it is associated with lowest incidence of

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morbidity and mortality, best long-term primary patency rate, and fewest complications, such as infection or clotting, compared to all other access choices like arteriovenous graft (AVG) or central venous catheter (CVC).<sup>3</sup>

For HD patients, blockages created by repeated access or narrowing of the blood vessel (restenosis) are a common problem and hinder treatment. Problems with vascular access are an important cause of morbidity and mortality in HD patients. In the United States, it has been estimated that US\$1 billion per year is spent on vascular access and its complications.<sup>4</sup> Some patients require up to eight reinterventions per year to maintain AVF function.<sup>5</sup> For patients undergoing HD for kidney failure, who already spend a significant portion of their time undergoing dialysis and other treatments, repeated reinterventions to maintain AV access can be an added burden.

Despite significant developments during the past years, outcomes of surgical arteriovenous fistulas (SAVFs) are still suboptimal. Complications, such as thrombosis, occur in 20% of cases, and 20%–60% of AVFs fail to mature.<sup>6–8</sup> A successful fistula requires an average of two additional catheter-based procedures to facilitate maturation, leading to delays until usable access is available.<sup>9</sup>

At present, two endovascular catheter-based systems, the WavelinQ™ 4F EndoAVF System (DB—Becton, Dickinson and Company, NJ, USA) and Ellipsys® Vascular Access System (Avenu Medical, San Juan Capistrano, CA, USA), have been developed to apply a minimally invasive method to create an AVF as an alternative to the traditional open surgical approach.<sup>10</sup> Ellipsys is a thermal resistance device that enables arteriovenous anastomosis of the proximal radial artery and perforating vein while WavelinQ works slightly differently as it is a dual catheter-based system that creates an AVF between arteries (typically the ulnar artery/radial artery) and veins (ulnar vein/radial vein) of the proximal forearm, offering two anatomic options for AVF creation. Endovascular technology, which allows fistula creation with minimal vessel trauma, showed encouraging outcomes with high technical success rates, low reintervention and failure rates, and good usability for HD.<sup>11</sup>

The overall aim of the present study was to measure the added value of endovascular catheter-based approach for the endovascular creation of AVF (endoAVF) with WavelinQ system in HD patients and to compare it to the surgical approach (SAVF), through a health technology assessment, to inform decision-makers in due course on the choices offered to HD patients in the context of access creation. In particular, the aim of the present study was to perform cost-effectiveness and budget impact analyses comparing endoAVF by WavelinQ to SAVF in HD patients from the Italian Healthcare Service perspective.

## Methods

### Retrieval of clinical efficacy data

With the aim of retrieving data to populate a cost-effectiveness model, a systematic literature review has been conducted for endoAVF and SAVF and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>12</sup> The search considered randomized controlled trials (RCTs), prospective clinical trials, and observational studies. While the latter have some limitations compared with RCTs, such studies can offer valuable real-world evidence on the use of the technology.<sup>13,14</sup>

A comprehensive search strategy to scan the four items within the PICO (Population: HD patients needing native AVF creation, Intervention: endoAVF, Comparator: SAVF, and Outcomes) framework has been designed and used in June 2019 to search PubMed and Web of Science scientific databases.

As regards the outcomes, the search focused mainly on complications after clinical interventions since they are directly linked with healthcare resource consumption (and consequently costs) to perform the economic evaluation. Studies reporting data on patients' quality of life have been searched as well.

Studies were considered if published in English and if they referred to an adult population. No restrictions were imposed on the location of the study, while the year of publication was limited to the last 10 years, considering the relatively recent development of the endoAVF approach. Case reports, letters, comments, editorials, and reviews were excluded. Two investigators (C.R. and M.T.) independently performed the screening on titles and abstracts, first, and full-texts later. Studies were excluded based on titles and abstract screening according to the following exclusion criteria: (a) no abstract available, (b) specific focus on pediatric or adolescent population, and (c) focus on interventions different from vascular access creation. Full-text articles were retrieved and reviewed by the same two investigators. Articles were excluded if they did not provide any data on rates of complications or quality of life. All search results were extracted in MS Excel software. Details on the search strategy are reported in the Appendix, while Table 1 reports the inclusion criteria.

Twenty-six studies have been found reporting data on the number of events following fistula creation. None of these studies reported data on patients' quality of life useful for cost-effectiveness analysis. A summary of main data is reported in Table 2 (see Supplemental Table 1 for detailed data).

Two studies,<sup>17,39</sup> which considered WavelinQ device, directly compared the two AVF creation procedures through propensity score matching (PSM) technique. On the remaining single-arm studies, sixteen, mainly retrospective, reported data on SAVF, while eight studies

**Table 1.** Inclusion criteria for the systematic literature review.

Population	Studies considering adult haemodialysis population needing native AVF creation
Intervention	EndoAVF
Comparator	SAVF
Outcome	Rates of complications, data on quality of life
Study	Randomized controlled trials (RCTs), prospective clinical trials, and observational studies
Availability	English; full text
Time and place	The search was limited to studies published in the last 10 years. Place limits were not set for this review.

AVF: arteriovenous fistula; SAVF: surgical arteriovenous fistula.

focused on endoAVF (four on WavelinQ and four on Ellipsys). The follow-up ranged from 4.6 to 84 months and the number of studied patients ranged from 73 to 33,091 for SAVF and from 8 to 107 for endoAVF.

Because comparative studies based on PSM have been considered the ones with higher data quality compared to single-arm investigations, these studies were evaluated for the model development for the economic evaluations. In particular, the first published study<sup>39</sup> considered a random sample from Medicare to determine post-creation procedures and associated costs for SAVF and compared them with data on endoAVF with WavelinQ from the Novel Endovascular Access Trial (NEAT).<sup>29</sup> However, information on incident and prevalent status could not be evaluated with Medicare. The second study<sup>17</sup> considered endoAVF (WavelinQ) data from the same NEAT trial, while data on SAVF were retrieved from the United States Renal Data System (USRDS). This study has carried out the comparative analysis between WavelinQ and surgical procedure by distinguishing incident and prevalent dialysis patients and it has been chosen as the source for developing the model in our study in order to perform the economic evaluations.

### Target population and events for the comparison between endoAVF (WavelinQ) and SAVF

Patients in the USRDS database were 13,265 adults who performed SAVF creation and enrolled in Medicare and followed for 6 months before and for 6 months after the AVF creation date. The endoAVF cohort considered the 60 participants enrolled in the NEAT study. Patients were defined as incident if they were not on dialysis at the time of AVF creation; all USRDS incident patients received dialysis.

A 1-1 PSM has been performed to compare event rates, intervention-free survival, and costs between endoAVF and SAVF cohorts, leading to a comparison of 27 and 33 for incident and prevalent patients, respectively.<sup>17</sup> Table 3 reports the rates of events distinguished by cohort and population.

### The model

A Markov model has been selected for this economic evaluation.<sup>41</sup> A Markov model comprises a finite set of health states in which an individual can be found. The states are such that in any given time interval, the individual will be in only one health state. In the original graphical representation of Markov models, sometimes referred to as a “bubble diagram”, each state is represented with a circle, while arrows represent transitions from one state to another. Movements among states are defined by transition probabilities. Transitions usually happen at fixed time intervals (Markov cycle). A transition arrow pointing back to the state from which it originates indicates that it is possible for an individual to remain in the same state for more than one cycle. Rewards are assigned to each health state and earned at the end of each cycle; in our case, the model projects quality adjusted life years (QALYs) and costs associated with endoAVF (WavelinQ) and SAVF for both incident and prevalent cohorts.

The health states considered in the implemented model were “native AVF, no events” and “complications” (Figure 1). A hypothetical cohort of patients starts the Markov process in the “native AVF no events” state. Patients may stay in the “native AVF no events” state or, in case of events, may move to the “complications” state. Transition probabilities between health states for incident/prevalent patients undergoing endoAVF or SAVF have been estimated from freedom from intervention curves presented in Arnold et al.<sup>17</sup> (Supplemental Table 2). Exponential functions have been fitted for the event-free curves emerging from the two matched cohorts according to treatment strategy. A Markov cycle length of 1-month and a horizon of 1 year have been chosen for baseline analysis.

The model was implemented using TreeAge Software (TreeAge Software, Inc., Williamstown, MA, USA).

### Healthcare resource consumption and costs

Direct healthcare resource consumption (direct costs) was considered in the model (Eur, 2019). Data on costs were obtained from national diagnosis-related groups (DRGs) reimbursement rates to reflect the Italian Healthcare System perspective (Table 4). For the endovascular procedure with WavelinQ, we assumed it can be performed in a day-hospital (DH) setting, while for the surgical one, the standard DRG tariff has been applied. Angioplasty has been considered as a DH procedure.

### Quality-of-life estimates

Health-related quality-of-life measures were not available from Arnold et al.<sup>17</sup> The utility coefficients for the main events have been retrieved from another publication, obtained by the systematic literature search, involving the same authors<sup>42</sup> which reported utility values for AVF

**Table 2.** Summary of study characteristics.

Study	Surgery or endovascular procedure	Device used for endoAVF	Study type	N. pts or AVF	On dialysis (%)	Country	Follow-up (months)
Ahmed et al. <sup>15</sup>	Surgery	–	Prospective, hospital-based study	73	97.30	Egypt	>8 weeks, not specified
Arhuidese et al. <sup>16</sup>	Surgery	–	Retrospective study	73,884	100	USA	21.9
Arnold et al. <sup>17</sup>	Both	WavelinQ	Propensity score matching	27 incident 33 prevalent	0 100	Canada, Australia, and New Zealand versus USA	12
Berland et al. <sup>18</sup>	Endo	WavelinQ	Single center, single-arm, prospective study	32	97	Paraguay	6
Bylsma et al. <sup>19</sup>	Surgery	–	Retrospective study	N pts = 33,091, N AVF = 38,035	100	USA	13 median
Chisci et al. <sup>20</sup>	Surgery	–	Retrospective study	317	NA	Italy	12
Fokou et al. <sup>21</sup>	Surgery	–	Retrospective study	628	100	Camerun	9.2 median
Fumagalli et al. <sup>22</sup>	Surgery	–	Retrospective cohort study	204	100	Italy	48.6
Hebibi et al. <sup>23</sup>	Endo	Ellipsys	Retrospective study	34	NA	France	14
Hemmati et al. <sup>24</sup>	Surgery	–	Retrospective study	176	100	Iran	NA
Hull et al. <sup>25</sup>	Endo	Ellipsys	Retrospective study	26	100	Mexico	12
Hull et al. <sup>26</sup>	Endo	Ellipsys	Prospective study	107	62	USA	12
Johny and Luther <sup>27</sup>	Surgery	–	Retrospective + prospective	118	100	India	9
Lee et al. <sup>28</sup>	Surgery	–	Retrospective study	694	80	Singapore	27.6
Lok and Rajan <sup>29</sup>	Endo	WavelinQ	Prospective single-arm multicenter study	60	43	Six sites in Canada and three sites in Australia and New Zealand	12
Mallios et al. <sup>30</sup>	Endo	Ellipsys	Prospective study	34	69	France	4.6
Mishler and Yevzlin <sup>31</sup>	Surgery	–	Retrospective analysis of a prospectively collected vascular access database	98	65	USA	9.5
Praehauser et al. <sup>32</sup>	Surgery	–	Retrospective cohort study	211	NA	Switzerland	48
Radosa et al. <sup>33</sup>	Endo	WavelinQ	Retrospective	8	0	Germany	6
Radoui et al. <sup>34</sup>	Surgery	–	Retrospective study	96	100	Morocco	12 min
Rajan et al. <sup>35</sup>	Endo	WavelinQ	Prospective study	33	0	Paraguay	6
Sahasrabudhe et al. <sup>36</sup>	Surgery	–	Retrospective observation study	247	NA	India	1–7 years
Schinstock et al. <sup>37</sup>	Surgery	–	Retrospective cohort study	293	84	USA	48
Xue et al. <sup>38</sup>	Surgery	–	Prospective study	4151	100	USA	12
Yang et al. <sup>39</sup>	Both	WavelinQ	Propensity score matching	60	NA	Canada, Australia, and New Zealand versus USA	12
Yoo et al. <sup>40</sup>	Surgery	–	Retrospective study	338	NA	Korea	7

AVF: arteriovenous fistula.

(0.614), AVG (0.566), and CVC (0.538). Because the reference study did not report the duration of events experienced by the patients, we calculated a mean utility value for the health state “complications” based on the reported

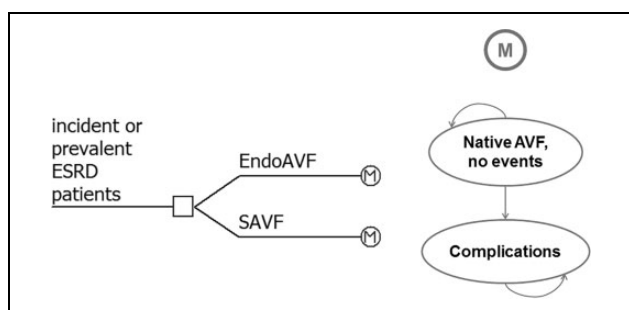
frequencies of events. We assumed that events related to the management of the fistula (e.g. thrombolysis, thrombectomy) caused a lowering of the patients’ quality of live for a limited time, and for this reason, these events were not

**Table 3.** Event rates per patient year for incident and prevalent patients (time horizon of 1 year).

	Incident patients		Prevalent patients	
	endoAVF <sup>a</sup> cohort (N = 27)	SAVF cohort (N = 27)	endoAVF <sup>a</sup> cohort (N = 33)	SAVF cohort (N = 33)
Inpatient vascular access–related infection	0	0.461	0.035	0.064
Outpatient vascular access–related infection	0	0.384	0	0.064
Thrombectomy	0.083	0.077	0	0.384
Revision	0.041	0.461	0.035	0.192
DRIL, for steal syndrome	0.041	0	0	0
Angioplasty	0.041	0.844	0.035	1.217
Catheter placement	0.124	3.07	0.106	0.512
AVG creation	0.041	0.384	0	0.64
New AVF or transposition	0.083	1.382	0.141	0.64
Thrombin injection	0.083	0	0	0
Embolization/ligation	0.207	0.077	0.071	0.192
Thrombolysis	0	0	0.035	0
Stent placement	0	0.077	0	0.192
Total event rate per patient (mean)	0.74	7.22	0.46	4.10

SAVF: surgical arteriovenous fistula; DRIL: distal revascularization and interval ligation; AVG: arteriovenous graft.

<sup>a</sup>WavelinQ device.

**Figure 1.** Model representation (M=Markov model).

accounted in the model. This approach led to the estimation of a utility coefficient of 0.568 and 0.562 for the “complication” health state for incident patients undergoing endoAVF and SAVF, respectively. The values for prevalent patients’ cohort were 0.581 and 0.575, respectively. A utility coefficient of 0.614 has been applied to the “native AVF, no events” health state.

### Cost-effectiveness analysis (CEA)

Costs and QALYs for the considered strategies were estimated to calculate the incremental cost–utility ratio (ICUR) of endoAVF (with WavelinQ device) versus SAVF. Considering the limited time horizon for the analysis (1 year), QALYs and costs were not discounted. Transition probabilities, costs, and utilities were entered into the model along with a distribution: beta for utilities and transition probabilities and gamma for costs (a standard deviation of 10% of the baseline value has been considered for all the distributions). Deterministic and probabilistic sensitivity analyses (PSA) were performed to test the robustness

of the model. In the latter case, second-order Monte Carlo simulations (10,000 iterations) were conducted for incident and prevalent cohorts to take into account parameters variability; resulting scatterplots were plotted onto a cost-effectiveness plane.

### Budget impact analysis

A budget impact model has been developed based on the cost-effectiveness analysis (CEA) model to evaluate the expected changes in the expenditure for the Italian Health-care Service in the hypothesis of an increased utilization of endoAVF with WavelinQ in place of SAVF for incident HD patients.

The annual incidence of HD in Italy accounts for about 9500 patients,<sup>43</sup> of which about 68% can be considered for AVF creation (6460).<sup>44</sup>

As the use in Italy of WavelinQ is at the beginning, the current scenario of patients’ distribution between the two alternative creation procedures considered 100% of use of SAVF. Future scenarios considered increased proportions of use of WavelinQ over SAVF of 0.5%, 2%, 4%, 6%, and 8% for the following 5 years. The model applies the variations of the market share to the new incident cohorts (naive treatments), without considering the prevalent cohort. Constant incident cohorts were considered in the analysis.

The costs for current and future scenarios were estimated by multiplying yearly costs of each option by the proportion of the eligible population using that option and by the number of patients in the eligible population, taking into account subsequent yearly incident cohorts. As the focus was on the expected budget at each point in

**Table 4.** DRGs reimbursement rates for the different procedures.

Procedure	DRG	National tariff
Inpatient vascular access–related infection	418 Postoperative and post-traumatic infections	€ 3508
Thrombectomy	479 Other vascular procedures W/O CC	€ 4742
Revision	120 Other circulatory system O.R. procedures	€ 6876
Distal revascularization and interval ligation (DRIL) for steal syndrome	120 Other circulatory system O.R. procedures	€ 6876
Angioplasty	479 Other vascular procedures W/O CC	€ 2258 (DH tariff)
Catheter placement (CVC)	145 Other circulatory system diagnoses W/O CC	€ 2097
AVG creation	120 Other circulatory system O.R. procedures	€ 6876
AVF creation or transposition	120 Other circulatory system O.R. procedures	EndoAVF € 2544 (DH tariff) SAVF € 6876
Thrombin injection	479 Other vascular procedures W/O CC	€ 4742
Embolization/ligation	479 Other vascular procedures W/O CC	€ 4742
Thrombolysis	145 Other circulatory system diagnoses W/O CC	€ 2097
Stent placement	145 Other circulatory system diagnoses W/O CC	€ 2097

DRG: diagnosis-related group; DH: day-hospital; AVG: arteriovenous graft; AVF: arteriovenous fistula; SAVF: surgical arteriovenous fistula; CVC: central venous catheter.

**Table 5.** Model results for incident and prevalent patients (time horizon 1 year).

	Incident patients		Prevalent patients	
	Costs	QALYs	Costs	QALYs
EndoAVF (WavelinQ)	5722€	0.607	3978€	0.608
SAVF	33,041€	0.589	24,178€	0.595

SAVF: surgical arteriovenous fistula; QALYs: quality adjusted life years.

time, the financial streams were presented as undiscounted costs.<sup>45</sup>

## Results

### CEA results

Considering a time horizon of 1 year, for WavelinQ, the average QALYs were estimated to be 0.607 for incident patients and 0.608 for prevalent patients; for SAVF, the average QALYs were 0.589 and 0.595 for the two populations considered. The mean costs per patient for WavelinQ were estimated to be 5722€ and 3978€ for incident and prevalent patients, respectively, while for SAVF costs of 33,041€ and 24,178€ were obtained, respectively.

For both incident and prevalent cohorts, endoAVF with WavelinQ was the dominant strategy (i.e. less costly and with higher QALYs) compared with SAVF. The model results for the two scenarios are summarized in Table 5.

A scenario analysis has been conducted by considering the standard DRG reimbursement for both WavelinQ and SAVF procedures. In this case, the mean costs per patient for WavelinQ were 10,414€ and 8920€ for incident and prevalent patients, respectively. These costs were still lower than the corresponding ones for SAVF and, for both cohorts, endoAVF with WavelinQ was confirmed as the dominant strategy.

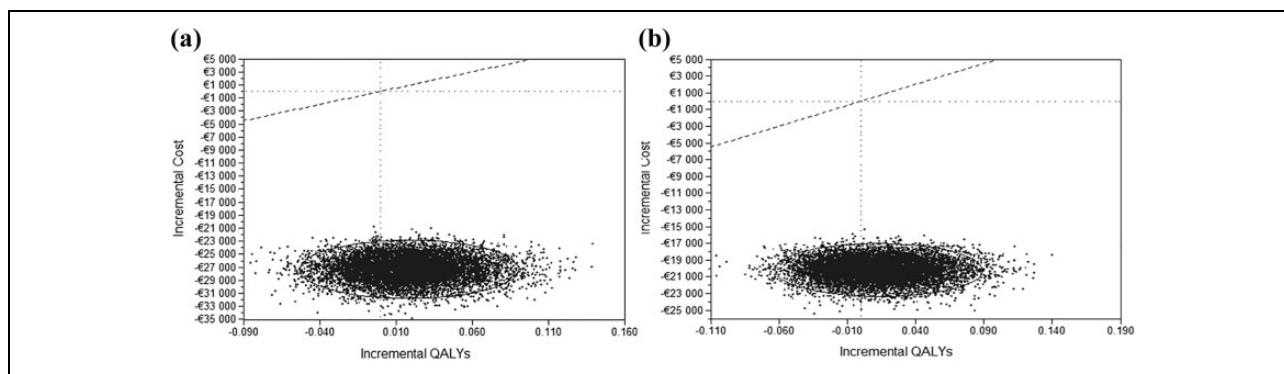
The plots of incremental costs versus incremental QALYs obtained from the Monte Carlo simulations are shown in Figure 2 (a: incident patients; b: prevalent patients). Dotted lines represent a theoretical cost-effectiveness threshold of 50,000€/QALY; the totality of points lie below this line for incident and prevalent cohorts, respectively.

### Budget impact analysis

In comparison with the current scenario (year 0), by progressively increasing endoAVF (WavelinQ) utilization rates for incident HD patients to 0.5%, 2%, 4%, 6%, and 8%, it would be possible to save 882,404€, 3,529,615€, 7,059,230€, 10,588,844€, and 14,118,459€ for 1-, 2-, 3-, 4-, and 5-year scenarios, respectively, yielding total savings of about 36 million euros over the next 5 years (Table 6). In the scenario that considered the standard DRG tariff for both WavelinQ and SAVF procedures, the total savings on a time horizon of 5 years would be about 30 million euros.

## Discussion

Patients with progressive renal insufficiency or renal failure have limited possibilities of receiving an organ from a donor, as the number of available kidney donors is significantly lower than the growing incidence of end-stage renal disease.<sup>46</sup> To replace the kidney function by HD, the endovascular creation of AVF has emerged as an option in addition to the surgical procedure. The surgical placement of an arteriovenous access alone is challenging and may be subject to complications. Even with a precise technique, vessel irritation, turn phenomena, or neointimal hyperplasia may occur, leading to early closure or disturbed maturation.<sup>7</sup> Moreover, patients requiring AVF



**Figure 2.** Scatterplot of incremental costs versus incremental QALYs obtained from Monte Carlo simulations for the comparison endoAVF versus SAVF for incident (a) and prevalent (b) cohorts.

**Table 6.** Budget impact analysis for incident HD patients.

	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Current scenario<sup>a</sup></b>						
% of treated patients with endoAVF	0	0	0	0	0	0
% of treated patients with SAVF	100	100	100	100	100	100
No. of treated patients with endoAVF	0	0	0	0	0	0
No. of treated patients with SAVF	6460	6460	6460	6460	6460	6460
Total budget impact endoAVF	€0	€0	€0	€0	€0	€0
Total budget impact SAVF	€213,444,860	€213,444,860	€213,444,860	€213,444,860	€213,444,860	€213,444,860
Total budget impact	€213,444,860	€213,444,860	€213,444,860	€213,444,860	€213,444,860	€213,444,860
<b>Future scenario<sup>a</sup></b>						
% of treated patients with endoAVF	0	0.5	2	4	6	8
% of treated patients with SAVF	100	99.5	98	96	94	92
No. of treated patients with endoAVF	0	32	129	258	388	517
No. of treated patients with SAVF	6460	6428	6331	6202	6072	5943
Total budget impact endoAVF	€0	€184,821	€739,282	€1,478,565	€2,217,847	€2,957,130
Total budget impact SAVF	€213,444,860	€212,377,636	€209,175,963	€204,907,066	€200,638,168	€196,369,271
Total budget impact	€213,444,860	€212,562,456	€209,915,245	€206,385,630	€202,856,016	€199,326,401
Savings	€0	-€882,404	-€3,529,615	-€7,059,230	-€10,588,844	-€14,118,459
<b>Total savings in 5 years</b>						<b>-€36,178,552</b>

HD: hemodialysis; SAVFs: surgical arteriovenous fistulas.

<sup>a</sup>EndoAVF refers to WavelinQ device.

access are usually old, with comorbidities and with poor vessel conditions, resulting in only few treatment options available. All these factors may cause high failure and high reintervention rates.<sup>47</sup>

EndoAVF creation is a sophisticated procedure providing a minimally invasive alternative to open surgical creation of AVF. This technique has been developed to address the limitations of surgical fistulas such as skin incision, vessel dissection, and the sutured anastomosis, which may result in prolonged healing, complications, and a low rate of functional fistula creation.<sup>4</sup> Furthermore, endoAVFs can be created in outpatient setting with local or regional anesthesia and sedation, and do not require the use of the operating theater. The proximal radial artery AVF created using an endovascular approach for the anastomosis showed excellent 2-year cumulative patency and a high level of patient satisfaction.<sup>48</sup>

Although endoAVF showed promising clinical efficacy with a good safety profile in published studies and registries,<sup>29,33</sup> the use of this option at present is not officially recommended over SAVF creation. Large RCTs comparing endoAVF to SAVF have not been implemented and no comparative results from these studies have been published so far. Since endoAVF uptake in clinical practice is growing in Italy and in other countries, the use of real-world data to support decision-making may be in these cases highly relevant.<sup>49,50</sup>

The present study aimed to evaluate the cost-utility of endoAVF versus SAVF and related budget impact at the national level to assess the value of currently available AVF creation procedures in the clinical practice in Italy. The analysis was performed using observational real-world data from a published study which compared WavelinQ versus surgical procedure for AVF creation.<sup>17</sup> Therefore,

our findings are not generalizable to the entire class of endoAVF devices but, instead, to WavelinQ only.

The results from this analysis suggest that endoAVF performed with WavelinQ could be a cost-saving strategy in comparison to SAVF for incident and prevalent HD patients, from an Italian Healthcare Service perspective. Furthermore, the probabilistic sensitivity analysis confirmed the results, with the totality of the simulations lying below the commonly accepted ICUR threshold representing value for money. Moreover, the BIA showed that the Italian Healthcare Service could save from 30 to 36 million euros in the hypothesis of an increased utilization of WavelinQ, from 0.5% to 8%, in place of SAVF in the next 5 years.

From our analyses, it emerged a great difference in costs for AVF creation and its management for the two considered procedures. This difference is mainly due to the lower number of complications occurring after the endovascular procedure compared to the surgical one. The reference study<sup>17</sup> used for the CEA model implementation reported for the matched incident HD patients an event rate of 0.74/person-year for endoAVF versus 7.22/person-year for SAVF ( $p < 0.0001$ ); similarly, in matched prevalent patients, the event rate was 0.46/person-year for endoAVF (WavelinQ) versus 4.10/person-year for SAVF ( $p < 0.0001$ ).

In literature, there is paucity of studies presenting cost-effectiveness or budget impact analyses comparing endoAVF to SAVF in HD patients. To our knowledge, only Yu et al.<sup>42</sup> performed a cost-effectiveness analysis using retrospective data in the United States comparing endovascular AVF creation with WavelinQ from the Novel Endovascular Access Trial with propensity score-matched SAVF procedures from the US Renal Data System for 1 year after AVF creation. That study showed that, excluding the cost of the device, endovascular AVF creation resulted in a cost-saving option compared with the surgical one for both incident and prevalent HD cohorts. These results are in line with the ones of our study; this means that the savings could be used (at least partially) to cover the costs of the technological innovation, thus leaving the Italian Healthcare Service cost neutral in the worst case, that is, if all savings should be reverted to cover the incremental costs of the innovative procedure.

The present study has a number of limitations. First of all, the clinical effectiveness was derived on the matched databases with a limited number of patients in the US context; therefore, the generalizability of the real-world patient data collected to the broader Italian HD population could not be verified. Moreover, a small sample of patients belonging to a single center (the NEAT study, 60 patients) was matched with a tiny percentage of patients belonging to the Renal Data System in United States ( $n = 13,265$ ). While the former group is composed by patients selected for endovascular AVF procedure according to best

anatomical findings, clinical/physical aspects, and ultrasound examinations, the surgical group, although matched through main variables related to clinical history, may represent a broad set of patients with variations in vessel quality, preoperative evaluation, and surgical expertise; this may have led to underlying differences on other aspects not considered in the matching process, thus possibly limiting the validity of this kind of analysis.

Second, costing for healthcare resource consumption was based on DRG reimbursement rates which, in general, especially in the context of use of medical devices, does not cover the actual cost of the procedure and materials. In Italy, the NHS acts as both third-party payer and provider of healthcare services. This means that—besides DRGs (i.e. tariffs level)—it might be important to estimate the actual production costs from the hospital perspective. This estimation could be important for hospitals, especially when procurement strategies and negotiations with the manufacturers are at stake, especially in times of growing interest in value-based procurement aimed at acquiring technologies whose benefits outweigh the extra costs. Third, since data on patients' quality of life were not available for the investigated population, assumptions have been made to populate the model health states with utility coefficients retrieved by literature. Moreover, worsening of patients' quality of life due to fistula management (e.g. thrombolysis, thrombectomy) has not been considered in the model, and this could have led to possible overestimations of patients' QALYs. Fourth, clinical outcomes and resource consumption related to patients managed with new technologies, such as endoAVF, may be influenced by the underlying learning curve related to the experience of the operators.<sup>51</sup> Continuous monitoring and data collecting could provide more robust data also for the evaluation of this aspect.

Finally, because the model used for the economic evaluations was developed according to published data comparing WavelinQ versus surgical procedure, the results of our analyses are valid only for this comparison, and no conclusions may be made on other endovascular devices. Further studies would be needed before our findings can be extended to other comparisons.

In conclusion, endoAVF with WavelinQ seems to be a valid option for the creation of HD venous access. Medical devices, which are subject to incremental innovation and operators' learning curve, present challenges with respect to drugs concerning their assessment process;<sup>52</sup> in this case, the production of real-world evidence can sometimes be more meaningful for policy makers in comparison with RCTs.<sup>51</sup> Future real-world studies comparing endoAVF to SAVF will be able to increase the clinical evidence to confirm or reject the validity of this preliminary evaluation, not only for WavelinQ but also for other possible endovascular devices for AVF. In the time being, decision-makers may base on these preliminary results



coverage recommendations for approval in defined target patient populations.

### Authors' note

No interferences occurred in carrying out the research project and in writing the manuscript for which the authors are the sole responsibility.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.


### Ethics statement

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### Supplemental material

Supplemental material for this article is available online.

### References

- Couser WG, Remuzzi G, Mendis S, et al. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney Int* 2011; 80(12): 1258–1270.
- <https://www.niddk.nih.gov/health-information/kidney-disease/kidney-failure/hemodialysis/vascular-access>
- Sidawy AN, Spergel LM, Besarab A, et al. The Society for Vascular Surgery: clinical practice guidelines for the surgical placement and maintenance of arteriovenous hemodialysis access. *J Vasc Surg* 2008; 48(5 Suppl.): 2S–25S.
- Roy-Chaudhury P, Sukhatme VP and Cheung AK. Hemodialysis vascular access dysfunction: a cellular and molecular viewpoint. *J Am Soc Nephrol* 2006; 17(4): 1112–1127.
- Vazquez-Padron RI and Allon M. New insights into dialysis vascular access: impact of preexisting arterial and venous pathology on AVF and AVG outcomes. *Clin J Am Soc Nephrol* 2016; 11(8): 1495–1503.
- Shenoy S. Surgical anatomy of upper arm: what is needed for AVF planning. *J Vasc Access* 2009; 10(4): 223–232.
- Al-Jaishi AA, Oliver MJ, Thomas SM, et al. Patency rates of the arteriovenous fistula for hemodialysis: a systematic review and meta-analysis. *Am J Kidney Dis* 2014; 63(3): 464–478.
- Huijbregts HJT, Bots ML, Wittens CHA, et al. Hemodialysis arteriovenous fistula patency revisited: results of a prospective, multicenter initiative. *Clin J Am Soc Nephrol* 2008; 3(3): 714–719.
- Falk A. Maintenance and salvage of arteriovenous fistulas. *J Vasc Interv Radiol* 2006; 17(5): 807–813.
- Steinke T, Rieck J and Nuth L. Endovascular arteriovenous fistula for hemodialysis access. *Gefässchirurgie* 2019; 24(Suppl. 1): S25–S31.
- Jones RG and Morgan RA. A review of the current status of percutaneous endovascular arteriovenous fistula creation for haemodialysis access. *Cardiovasc Intervent Radiol* 2019; 42(1): 1–9.
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; 339: b2535.
- Tarricone R, Torbica A and Drummond M. Key recommendations from the MedtechHTA Project. *Health Econ* 2017; 26(Suppl. 1): 145–152.
- Berger ML, Sox H, Willke RJ, et al. Good practices for real-world data studies of treatment and/or comparative effectiveness: recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. *Value Health* 2017; 20(8): 1003–1008.
- Ahmed GM, Mansour MO, Elfatih M, et al. Outcomes of arteriovenous fistula for hemodialysis in Sudanese patients: single-center experience. *Saudi J Kidney Dis Transpl* 2012; 23(1): 152–157.
- Arhuidese IJ, Orandi BJ, Nejm B, et al. Utilization, patency, and complications associated with vascular access for hemodialysis in the United States. *J Vasc Surg* 2018; 68(4): 1166–1174.e2.
- Arnold RJG, Han Y, Balakrishnan R, et al. Comparison between surgical and endovascular hemodialysis arteriovenous fistula interventions and associated costs. *J Vasc Interv Radiol* 2018; 29(11): 1558–1566.
- Berland TL, Clement J, Griffin J, et al. Endovascular creation of arteriovenous fistulae for hemodialysis access with a 4 Fr device: clinical experience from the EASE study. *Ann Vasc Surg* 2019; 60: 182–192.
- Bylsma LC, Reichert H, Gage SM, et al. Clinical outcomes of arteriovenous access in incident hemodialysis patients with Medicare coverage, 2012–2014. *Am J Nephrol* 2019; 49(2): 156–164.
- Chisci E, Harris LM, Menici F, et al. Outcomes of three types of native arteriovenous fistula in a single center. *J Vasc Access* 2017; 18(5): 379–383.
- Fokou M, Teyang A and Ashuntantang G. Complications of arteriovenous fistula for hemodialysis: an 8-year study. *Ann Vasc Surg* 2012; 26(5): 680–684.
- Fumagalli G, De Pietro S, Migliori M, et al. Outcomes of vascular access care and surgery managed by interventional nephrologists: a twelve-year experience. *Blood Purif* 2016; 42(2): 111–120.

23. Hebib H, Achiche J, Franco G, et al. Clinical hemodialysis experience with percutaneous arteriovenous fistulas created using the Ellipsys<sup>®</sup> vascular access system. *Hemodial Int* 2019; 23(2): 167–172.
24. Hemmati H, Khosravi M, Heidarzadeh A, et al. Vascular access and survival in hemodialysis patients in Rasht, Iran. *Iran J Kidney Dis* 2011; 5(1): 34–37.
25. Hull JE, Elizondo-Riojas G, Bishop W, et al. Thermal resistance anastomosis device for the percutaneous creation of arteriovenous fistulae for hemodialysis. *J Vasc Interv Radiol* 2017; 28(3): 380–387.
26. Hull JE, Jennings WC, Cooper RI, et al. The pivotal multicenter trial of ultrasound-guided percutaneous arteriovenous fistula creation for hemodialysis access. *J Vasc Interv Radiol* 2018; 29(2): 149–158.e5.
27. Johny S and Luther A. Outcome of arteriovenous fistula for haemodialysis access. *J Evolution Med Dent Sci* 2018; 7(3): 361–366.
28. Lee KG, Chong TT, Goh N, et al. Outcomes of arteriovenous fistula creation, effect of preoperative vein mapping and predictors of fistula success in incident haemodialysis patients: a single-centre experience. *Nephrology* 2017; 22(5): 382–387.
29. Lok CE and Rajan DK. Usability of the endovascular arteriovenous fistula: 6m Results of the NOVEL Endovascular Access Trial (NEAT). *J Am Soc Nephrol* 2016; 27: 31A.
30. Mallios A, Jennings WC, Boura B, et al. Early results of percutaneous arteriovenous fistula creation with the Ellipsys Vascular Access System. *J Vasc Surg* 2018; 68(4): 1150–1156.
31. Mishler R and Yevzlin AS. Outcomes of arteriovenous fistulae created by a U.S. interventional nephrologist. *Semin Dial* 2010; 23(2): 224–228.
32. Praehauser C, Breidhardt T, Moser-Bucher CN, et al. The outcome of the primary vascular access and its translation into prevalent access use rates in chronic haemodialysis patients. *Clin Kidney J* 2012; 5(4): 339–346.
33. Radosa CG, Radosa JC, Weiss N, et al. Endovascular creation of an arteriovenous fistula (endoAVF) for hemodialysis access: first results. *Cardiovasc Intervent Radiol* 2017; 40(10): 1545–1551.
34. Radoui A, Lyoussfi Z, Haddiya I, et al. Survival of the first arteriovenous fistula in 96 patients on chronic hemodialysis. *Ann Vasc Surg* 2011; 25(5): 630–633.
35. Rajan DK, Ebner A, Desai SB, et al. Percutaneous creation of an arteriovenous fistula for hemodialysis access. *J Vasc Interv Radiol* 2015; 26(4): 484–490.
36. Sahasrabudhe P, Dighe T, Panse N, et al. Retrospective analysis of 271 arteriovenous fistulas as vascular access for hemodialysis. *Indian J Nephrol* 2013; 23(3): 191–195.
37. Schinstock CA, Albright RC, Williams AW, et al. Outcomes of arteriovenous fistula creation after the Fistula First Initiative. *Clin J Am Soc Nephrol* 2011; 6(8): 1996–2002.
38. Xue H, Ix JH, Wang W, et al. Hemodialysis access usage patterns in the incident dialysis year and associated catheter-related complications. *Am J Kidney Dis* 2013; 61(1): 123–130.
39. Yang S, Lok C, Arnold R, et al. Comparison of post-creation procedures and costs between surgical and an endovascular approach to arteriovenous fistula creation. *J Vasc Access* 2017; 18(Suppl. 2): 8–14.
40. Yoo DW, Yoon M and Jun HJ. Successful access rate and risk factor of vascular access surgery in arm for dialysis. *Vasc Specialist Int* 2014; 30(1): 33–37.
41. Briggs A and Sculpher M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics* 1998; 13(4): 397–409.
42. Yu TM, Tang J, Tradonsky AN, et al. Vascular access outcomes: impact on quality of life and associated costs following surgical or endovascular arteriovenous fistula creation for hemodialysis patients. *Value Health* 2018; 21(1): S162–S163.
43. Nordio M, Limido A, Conte F, et al. Report del Registro Italiano di Dialisi e trapianto relativo agli anni 2011-2013. *G Ital Nefrol* 2016; 33(3), <https://giornaleitalianodinefrologia.it/2016/06/report-del-registro-italiano-di-dialisi-e-trapianto-relativo-agli-anni-2011-2013/>
44. <https://www.dopps.org/>
45. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health* 2014; 17(1): 5–14.
46. Lozano RN. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380(9859): 2095–2128.
47. Vascular Access 2006 Work Group. Clinical practice guidelines for vascular access. *Am J Kidney Dis* 2006; 48(Suppl. 1): S176–S247.
48. Beathard GA, Litchfield T and Jennings WC. Two-year cumulative patency of endovascular arteriovenous fistula. *J Vasc Access*. Epub ahead of print 28 September 2019. DOI: 10.1177/1129729819877780.
49. Tarricone R, Torbica A, Ferre F, et al. Generating appropriate clinical data for value assessment of medical devices: what role does regulation play? *Expert Rev Pharmacoecon Outcomes Res* 2014; 14(5): 707–718.
50. Tarricone R, Boscolo PR and Armeni P. What type of clinical evidence is needed to assess health technologies. *Eur Respir Rev* 2016; 25: 259–265.
51. Tarricone R, Callea G, Ogorevc M, et al. Improving the methods for the economic evaluation of medical devices. *Health Econ* 2017; 26(Suppl. 1): 70–92.
52. Drummond M, Griffin A and Tarricone R. Economic evaluation for devices: same or different? *Value Health* 2009; 12(4): 402–404.