National Institute for Health and Care Excellence

IP1833 Percutaneous endovascular forearm-arteriovenous fistula creation for haemodialysis access

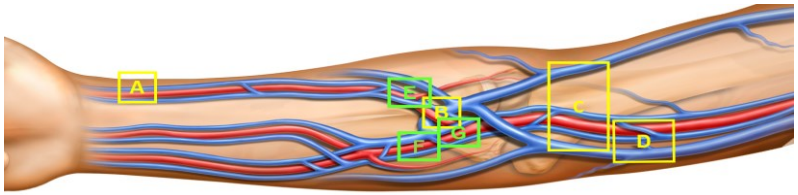
IPAC date: 12 August 2021

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 2 Royal College of Physicians and Surgeons of Glasgow	1.1 General Comments	The Royal College of Physicians and Surgeons of Glasgow although based in Glasgow represents Fellows and Members throughout the United Kingdom. While NICE has a remit for England, many of the recommendations are applicable to all devolved nations including Scotland. They should be considered by the relevant Ministers of the devolved governments. The College encourages research into new procedures which may benefit patients and streamline services to make them more effective. Our expert reviewer considered the document reasonable. This is a promising procedure but at this time an unproven surgical technique. We therefore consider it should only be used in an approved study with collection of results in a systematic way and should not be used in ordinary practice currently. Its effectiveness should be considered against existing methods of developing A-V fistulae.	Thank you for your comments. Special arrangements guidance requires the clinician to tell the patient about the uncertainties regarding the safety and efficacy of the procedure and collect further data by means of audit or research. **Section 1.6** in the draft guidance has been amended suggesting 'further research preferably in the form of randomised controlled trials'.
2	Consultee 3 BD, manufacturer	1.1	The draft guidance proposes a 'special arrangements' recommendation on the basis that evidence on efficacy is limited in quantity and quality. We submit that the guidance and the overview on which it is based does not take proper account of the quantity and	Thank you for your comments. The Committee considered this comment but decided not to change the guidance. Special arrangements guidance is not intended to be restrictive on the

			quality of the literature on percutaneous endovascular forearm arteriovenous fistula (endoAVF) in relation to the quantity and quality of the literature on the de facto alternative, surgical forearm arteriovenous fistula (SAVF) creation for haemodialysis (HD) access. EndoAVF is an additional option for AVF creation, but in a clinical situation, patients and their doctors will typically be considering vascular access for HD will be making a choice between endoAVF and SAVF: the relative quality of studies, outcomes measured, and length of follow-up for the two procedures are therefore germane. We submit that the quality of literature on endoAVF is similar to that on SAVF. We also submit that the guidance and the overview on which it is based does not consider the benefits of the procedure compared with the surgical alternative, specifically: • Improved cosmesis, as both a patient benefit and as an aid to patient acceptance of AVF, or earlier acceptance of AVF, as recommended in generally accepted guidance on HD vascular access. The committee will wish to note that the aesthetics of an AVF is important to patients: 'improves the aesthetics of the fistula which many patients report as extremely important to them (they don't want 'those lumps' on their arms) and which is likely to have really important quality of life benefits, less invasive surgery and the likelihood of minimal scarring following the procedure'; • By providing an additional site for AV access, endoAVF provides a distal alternative for patients in whom wrist/snuffbox or radiocephalic AVF (rcAVF) is impossible or difficult due to the patient's vascular anatomy in that area, for whom brachiocephalic AVF (bcAVF) or brachiobasilic (bbAVF) is the alternative. Patients with an endoAVF which fails to mature or becomes subsequently unusable retain the option of a bcAVF or bbAVF (with or without transposition) in the non-dominant arm;	procedure being performed or the patient having access to it. However, it requires the clinician to tell the patient about the uncertainties regarding the safety and efficacy of the procedure and collect further data by means of audit or research. NICE also encourages further research into the procedure in section 1.6 and may update this guidance on publication of further evidence. Some of the points raised about the benefits of the procedure are covered in different sections in the draft guidance. • Aesthetics of AVF is covered in section 3.8 of the guidance. • Additional sites for AV access are mentioned in procedure description (section 2.3) in the guidance. • Benefits and adverse events are presented in the rapid review of the published literature on the efficacy and safety of this procedure in the overview.

			• Reduced risk of trauma to the AV access vessels than the surgical alternative for which there are strong theoretical reasons for expecting earlier functional maturation and fewer interventions to achieve a functional result and maintain patency; • Lower blood flow in the resulting AVF than in the surgical alternatives (which uses dual outflow into the cephalic and basilic veins), resulting in fewer haemodynamic complications such as dialysis-access steal syndrome (DASS) and high-output heart failure, and means that two-needle cannulation is often possible at an earlier stage, shortening the time when a patient may require bridging vascular access with its known disadvantages. For these reasons, explored in detail below, we submit that guidance should be 'standard arrangements'. A 'special arrangements' recommendation is unnecessarily restrictive and is likely to inhibit patient access to the advantages of an alternative to the current standard procedure. This is particularly problematic in the case of a procedure which is effectively non-optional, in respect of which the literature indicates that patient resistance is a significant factor in delaying adoption of the recommended gold standard for vascular access and, in some cases, the permanent choice of a substandard option. We welcome the other recommendations in the draft guidance.	
3	Consultee 3 BD, manufacturer	2.2	We submit that the context in the guidance and the overview is incomplete. Renal replacement therapy (RRT) is a non-optional treatment for end-stage renal disease. Where AV access is required, permanently or as a bridge to transplant, there is a general consensus that AVF is the most desirable AV access on the basis that they have superior patency, fewer complications, require fewer reinterventions, and improved patient survival than alternatives (AV grafts and central venous catheters[1-6]). However, the guidance should	Thank you for your comments. Section 2.2 is intended to be a simple summary of current treatments for the condition (specified in section 2.1) and has been amended.

			recognise that even in the best hands AVFs, whether surgical or percutaneous, are not free of problems: • They may not mature (i.e., develop sufficient blood flow and structural strength to provide satisfactory access); • They may require secondary procedures such as basilic vein embolization, transposition, and embolisation of a tributary vein in order to assist maturation; Once mature, they may develop complications such as thrombosis, stenosis, steal syndrome, infection, aneurysms, pseudoaneurysms, high output cardiac failure, and hand ischaemia.	
4	Consultee 3 BD, manufacturer	2.2	The guidance and the overview do not take proper account of the clinical implications of the differing anatomy of endoAVF and SAVF procedures. There is a general consensus that AV access should be attempted as distal as possible in the forearm[3,7-11], so that a more proximal site can be used if the earlier site is, or becomes, unusable: initial access at the wrist, progressing proximally in the forearm and into the upper arm as additional access points are required[1,10,12]. This has to be balanced against the higher primary failure rate and shorter duration of patency of than an AVF created in the upper arm[13,14], especially in the elderly patient[4,15-18]. As a result there has been some movement away from rcAVFs[19], and the proportion of rcAVFs in two large trials has fallen from 54%[20] to 24%[21]. There is a price to pay for this: the incidence of DASS, arm oedema, high-output cardiac failure, the development of an aneurysm, haemodialysis access-related distal ischaemia (HAIDI) and idiopathic monomelic neuropathy[10,22-34]: this is thought to be due to the higher blood flow rate through the brachial artery than more distal arteries. EndoAVFs are performed in the majority of cases at locations in the proximal forearm (see figure) below the rcAVF and bb/bcAVFs. These offer some of the advantages of rcAVF while avoiding some of the disadvantages of bbAVFs and bcAVFs. A relatively little used surgical option using the radial	Thank you for your comments. Section 2 is intended to be a high-level overview of the indication (2.1), current treatments (2.2) and the procedure (2.3). It is not intended to be a detailed description of all the surgical options and techniques. Section 2.2 has been amended.

			artery (proximal radial artery AVF, praAVF) has been shown to have a lower complication rate and higher primary, assisted primary, and cumulative patency rates than the rcAVF[23,24,29,35-38] especially in elderly[22] and paediatric patients[39]. Unlike a surgical AVF, endoAVF does not require vein tributaries at the lower level of the perforating vein of the elbow to be ligated: this allows the maintenance of venous flow in case of occlusion of the anastomosis and simplifies salvage[40]. EndoAVFs establish a moderate-flow AVF between the proximal radial artery and the shared venous drainage with a low-pressure AVF that has adequate inflow for dialysis with lower turbulence and pressure in the outflow veins than a more proximal AVF. These qualities seem to be similar to the 'gold standard' distal surgical rcAVF[41].  *Yellow boxes are existing SAVF sites: A = radial artery-cephalic vein, B = proximal radial artery (PRA, little used)-perforating vein of the elbow PVE), C = brachial artery-cephalic vein, D = brachial artery-basilic vein. Green boxes are endoAVF sites: E = radial artery-radial vein, F = ulnar artery-ulnar vein, G = PRA-AVF* References: 1. NKF-K/DOQI, *National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for hemodialysis adequacy, update 2006.* Am J Kidney Dis, 2006. **48**: p. S2-S90. 2. Vascular Access Work, G., *Clinical practice guidelines for vascular access.* Am J Kidney Dis, 2006. **48 Suppl 1**: p. S248-73.	

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			Access System, technical recommendations, and an algorithm for maintenance. Journal of Vascular Surgery, 2020. **72**(6): p. 2097-2106.	
5	Consultee 3 BD, manufacturer	2.2	The guidance and the overview do not consider some relevant constraints on the current surgical options. Lack of suitable vasculature for an rcAVF is a problem in a significant number of patients, for whom endoAVF offers a valuable option. A study of a single cohort of 58 patients (116 arms) to establish suitability for rcAVF and endoAVF using manufacturer's instructions for use and published anatomical guidelines found only 32% were suitable for rcAVF, 93% for WavelinQ, and 52% for the Ellipsys[42]. Using a clinical algorithm with a preference for rcAVF creation, followed by endoAVF (pAVF) creation, SAVF creation at the elbow, and finally graft placement predicted initial rcAVF creation for 31% of the cohort, WavelinQ 32%, Ellipsys 23%, surgical fistula creation at the elbow 18%, and AVG 17%[42]. The WavelinQ NEAT (Novel Endovascular Access Trial) study reported 75% of eligible patients met the anatomic criteria for inclusion[43]. References: 42. Popli, K., et al., *Anatomic suitability for commercially available percutaneous arteriovenous fistula creation systems.* Journal of Vascular Surgery, 2021. **73**(3): p. 999-1004. 43. Lok, C.E., et al., *Endovascular Proximal Forearm Arteriovenous Fistula for Hemodialysis Access: Results of the Prospective, Multicenter Novel Endovascular Access Trial (NEAT).* Am J Kidney Dis, 2017. **70**(4): p. 486-497.	Thank you for your comments. Section 2.2 is intended to be a high-level overview of current treatments for the condition (specified in section 2.1) and has been amended. The overview considered the 2 studies (on anatomic suitability). Reference 42 (Popli 2021) has been included in the appendix in the overview. Reference 43 (Lok 2017, NEAT trial) was included in the systematic review (Yan Wee 2020) added to the summary of evidence.
6	Consultee 1 Medtronic	**2.3**	We suggest amending the following wording to reflect better the two techniques and devices used in this procedure. Specifically, we propose amending the highlighted text to: “The procedure can be performed by two different systems and is usually done in an outpatient setting under local anaesthesia or conscious sedation.”	Thank you for your comments. Section 2.3 has been amended.

			“A tiny needle is used to puncture the skin in the proximal forearm using ultrasound or fluoroscopic guidance. Depending on the system employed, 1 or 2 thin, flexible, specifically designed catheters…” “The catheters are aligned close to each other (using inbuilt magnets or mechanically approximated, depending on the system).”	
7	Consultee 1 Medtronic	**3.1**	Medtronic acknowledges the rapid evidence review of the published literature related to this procedure. We would like the IPAC to consider a recent publication (March 2021) comparing Ellipsys percutaneous arteriovenous fistula (AVF) creation with proximal forearm Gracz-type surgical AVF creation. The study groups included 89 percutaneous AVFs and 69 surgical AVFs, and both groups displayed high technical success rates and secondary patency. In addition, the study captured certain key efficacy and safety outcomes identified by NICE in this guidance, such as AVF patency, function, complications. It demonstrated that when a distal radial artery AVF is not feasible, percutaneous AVF may offer an appropriate procedure for creating safe and functional access, maintaining further proximal forearm surgical AVF creation options. Therefore, we kindly ask that this study be included in the evidence review. It enhances the quality and quantity of evidence verifying the additional benefit of percutaneous endovascular forearm AVF creation for haemodialysis access. **Reference:** Shahverdyan R, Beathard G, Mushtaq N, Litchfield TF, Vartanian S, Konner K, Jennings WC. Comparison of Ellipsys Percutaneous and Proximal Forearm Gracz-Type Surgical Arteriovenous Fistulas. American Journal of Kidney Diseases. 2021 Mar 1.	Thank you for your comments. The recent publication (Shahverdyan 2021) was identified in our update searches and has been added to the appendix in the overview as similar studies were included in the summary of key evidence section.
8	Consultee 1 Medtronic	**3.1**	Medtronic would like the IPAC to acknowledge that long term follow-up data is currently being studied as part of our evidence publication strategy. Accordingly, we would like the IPAC to consider a draft manuscript, awaiting journal	Thank you for your comments. The committee considered “academic and in confidence data” for safety issues but could not consider it for efficacy as

			submission in due course, provided as 'academic in confidence'. [ACADEMIC IN CONFIDENCE] IP1833	the data is not yet peer-reviewed and accepted for publication. The NICE IP programme manual states that efficacy outcomes from unpublished studies are not normally presented to the Committee. When substantial new evidence is published NICE will review the guidance.
9	Consultee 3 BD, manufacturer	**3.1** **'List of studies' (overview, p.12)**	Two recently published papers are relevant to the evidence review and should be included: (references 53, 54) 1. Shahverdyan R et al. Comparison of Ellipsys Percutaneous and Proximal Forearm Gracz-Type Surgical Arteriovenous Fistulas. American journal of kidney diseases: the official journal of the National Kidney Foundation, 2021. 01. 2. Osofsky R et al. Initial Outcomes Following Introduction of Percutaneous Arteriovenous Fistula Program with Comparison to Historical Surgically Created Fistulas. Annals of Vascular Surgery, 2021. We submit that the paper by Zemela (Zemela MS et al. Real-World Usage of the WavelinQ EndoAVF System. Ann Vasc Surg 2021; 70:116–22) should not have been excluded.	Thank you for your comments. The 2 studies (Shahverdyan 2021, Osofsky 2021) have been identified in our update search and have been added to the appendix in the overview. The study by Zemela 2021 has not been excluded. It is included in the appendix of the overview as larger studies were included in the summary of evidence.
10	Consultee 3 BD, manufacturer	**'Validity and generalisability of the studies', Overview, p.36**	In a systematic review of the vascular access outcomes and outcome measures used in 168 contemporary (January 2011 onwards) HD trials and trial protocols, n=1426 outcome measures were identified[44]. The three outcomes most frequently reported were function (136/168, 81% trials), infection (63/168, 38% trials), and maturation (31/168, 18% trials). Quality of life was reported in 5/168 (3%) trials, patient satisfaction in 2/168 (1%) trials, and needle phobia in 1/168 (0.6%) trials. As Viecelli and her colleagues observe 'there is	Thank you for your comments. The 'validity and generalizability of the studies' section in the overview highlights the limitations of the evidence base. The committee did not state that the evidence for endovascular AVF should be better than surgical AVF. Only evidence on efficacy and safety for endovascular AVF procedure was assessed in this guidance and most of the evidence included was from observational studies.

			substantial variability and inconsistency in vascular access outcomes and outcome measures reported in haemodialysis trials, with very little focus on patient-reported outcomes, making it difficult for clinicians, patients, and policy makers to make informed decisions.' We submit that it would be unreasonable for the committee to expect evidence in support of endoAVF to be substantially better than that available for the de facto alternative procedure, SAVF. An evidence-based clinical practice guideline for choosing a HD vascular access strategy developed by the Society for Vascular Surgery (SVS)[12] based on three systematic reviews[45-47], acknowledges the lack of high-quality evidence and comparative studies. A further system review including 200 studies published 8 years later stated that the 'results of this review are inherently limited by the quality of the primary included studies. Most of the studies included were observational studies and noncomparative.'[4] References: 44. Viecelli, A.K., et al., *Vascular Access Outcomes Reported in Maintenance Hemodialysis Trials: A Systematic Review.* American Journal of Kidney Diseases, 2018. **71**(3): p. 382-391. 45. Casey, E.T., et al., *Surveillance of arteriovenous hemodialysis access: a systematic review and meta-analysis.* J Vasc Surg, 2008. **48**(5 Suppl): p. 48S-54S. 46. Murad, M.H., et al., *Timing of referral for vascular access placement: a systematic review.* J Vasc Surg, 2008. **48**(5 Suppl): p. 31S-3S. 47. Murad, M.H., et al., *Autogenous versus prosthetic vascular access for hemodialysis: a systematic review and meta-analysis.* J Vasc Surg, 2008. **48**(5 Suppl): p. 34S-47S.	Therefore, section 1 in the guidance highlighted that ''evidence on its efficacy is limited in quantity and quality' and further research was recommended in 1.6.

			12. Sidawy, A.N., 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): p. 2S-25S. 4. Almasri, J., et al., *Outcomes of vascular access for hemodialysis: A systematic review and meta-analysis.* J Vasc Surg, 2016. **64**(1): p. 236-43.	
11	Consultee 3 BD, manufacturer	'Validity and generalisability of the studies', Overview, p.36	In relation to the statement that 'none of [the included] studies reported data on quality of life', we draw the committee's attention to the fact that Beathard 2020[48] does in fact include data from a patient satisfaction survey and a focus group, although it does not formally evaluate quality of life. We also draw the committee's attention to the fact that only 5/168 (3%) of SAVF trials do so[44]. We submit that it would be unreasonable for the committee to draw the conclusion that the evidence base for endoAVF was comparatively deficient in this respect: a patient and a clinician are necessarily making a choice between SAVF and endoAVF and must necessarily compare the quality and quantity of evidence for these two alternatives. References: 44. Viecelli, A.K., et al., *Vascular Access Outcomes Reported in Maintenance Hemodialysis Trials: A Systematic Review.* American Journal of Kidney Diseases, 2018. **71**(3): p. 382-391. 48. Beathard, G.A., T. Litchfield, and W.C. Jennings, *Two-year cumulative patency of endovascular arteriovenous fistula.* Journal of Vascular Access, 2020. **21**(3): p. 350-356.	Thank you for your comments. The study by Beathard 2020 (reference 48) has been included in the summary of evidence in the overview. The 'validity and generalizability of the studies' section in the overview highlights the limitations of the evidence base such as lack of data on quality of life. The committee did not state that the evidence for endovascular AVF should be better than surgical AVF. Only evidence on efficacy and safety for endoAVF procedure was assessed in this guidance and most of the evidence included was from observational studies and lacked data on quality of life. Therefore, section 1 in the guidance highlighted that ''evidence on its efficacy is limited in quantity and quality' and further research was recommended in 1.6 to focus on this.
12	Consultee 3 BD, manufacturer	**'Validity and generalisability of the**	The overview states that 'there are no randomised controlled trials comparing the effect of percutaneous endoAVF creation with SAVF creation for HD access in patients with end-stage kidney disease'. A search of MEDLINE and Embase carried	Thank you for your comments. The 'validity and generalizability of the studies' section in the overview only

		studies', Overview, p.36	out in early June 2021 with no date limitations found only 4 references to RCTs comparing vascular access procedures, 3 testing the value of CVCs vs. AVFs in elderly patients[49-51], a protocol for an RCT of immediate access AVG vs. tunnelled CVCs[52]. A search on the clinicaltrials.gov site found details of protocols for a further three RCTs comparing vascular access sites, two comparing AVF with AVG in elderly patients (NCT02981706 and NCT03545113), one comparing immediate-access with standard AVGs (NCT04388397), and one comparing the incidence of steal syndrome in two antecubital fossa AVF techniques (brachial artery inflow vs proximal radial or ulnar artery as inflow) (NCT02297451). The committee will note that neither the existing literature nor ongoing studies include RCTs of different SAVF techniques, with the limited exception of NCT02297451. The literature on which SAVF guidelines and clinical practice are based is observational. While recognising that RCTs are desirable, we submit that this is not in practice a reasonable criticism of the endoAVF evidence base. References: 49. Quinn, R., P. Ravani, and A.H. Investigators, *ACCESS HD pilot: A randomised feasibility trial Comparing Catheters with fistulas in Elderly patientS Starting haemodialysis.* BMJ Open. **6**(11): p. e013081. 50. Aitken, D.E.L., P.C. Thomson, and D. Kingsmore, *A randomised controlled trial of early cannulation grafts (ECAVGS) versus tunneled central venous catheters in patients requiring urgent vascular access for haemodialysis: One year follow-up.* Journal of the American Society of Nephrology, 2017. **28**: p. 48. 51. Branger, B., et al., *[Tunnelled internal jugular vein catheters with taurolidine lock: an acceptable challenge to arterio-venous fistula in 70 years old haemodialyzed patients: a prospective pilot study].* Nephrologie et Therapeutique. **7**(4): p. 237-41. 52. Aitken, E., et al., *Immediate access arteriovenous*	highlights the limitations of the evidence base such as lack of RCTs. The committee did not state that the evidence for endovascular AVF should be better than surgical AVF. Only evidence on efficacy and safety for endoAVF procedure was assessed in this guidance and most of the evidence included was from observational studies. Therefore, section 1 in the guidance highlighted that ''evidence on its efficacy is limited in quantity and quality' and further research preferably in the form of randomised controlled trials was recommended in 1.6.

			grafts versus tunnelled central venous catheters: study protocol for a randomised controlled trial. Trials [Electronic Resource]. **16**: p. 42.	
13	Consultee 3 BD, manufacturer	**'Validity and generalisability of the studies', Overview, p.36**	The overview states 'Follow-up periods varied across studies and was 6 to 12 months in many studies. Only 1 study had a 2-year follow up. There is a lack of long-term follow-up data'. The figure below shows the time points at which outcome measures of vascular access function for SAVFs are reported (Figure 1)[44]. The figure is based on n=136 trials. The committee will note that the majority of reports are at less than one year following AVF creation, and very few are reported more than three years after AVF creation. The follow-up in the studies reviewed by the committee (shown in Table 1) are not dissimilar from the findings reported by Viecelli[44] (Figure 1). We submit that the follow-up in the endoAVF evidence base is, given the context, adequate. Figure 1: Most frequently reported outcome measures (definitions and time points) to assess vascular access function (136 trials, 23 of 489 outcome measures) *Source: Viecelli 2018[44]*	Thank you for your comments. The 'validity and generalizability of the studies' section in the overview only highlights the limitations of the evidence base such as lack of long-term data. The committee did not state that the evidence for endovascular AVF should be better than surgical AVF. Only evidence on efficacy and safety for endoAVF procedure was assessed in this guidance and most of the evidence included was from observational studies and lacked long term data. Therefore, section 1 in the guidance highlighted that ''evidence on its efficacy is limited in quantity and quality' and further research was recommended in 1.6.

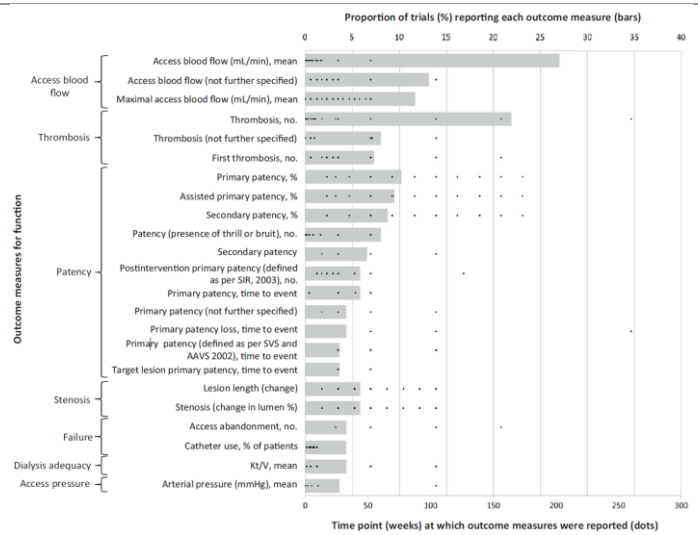
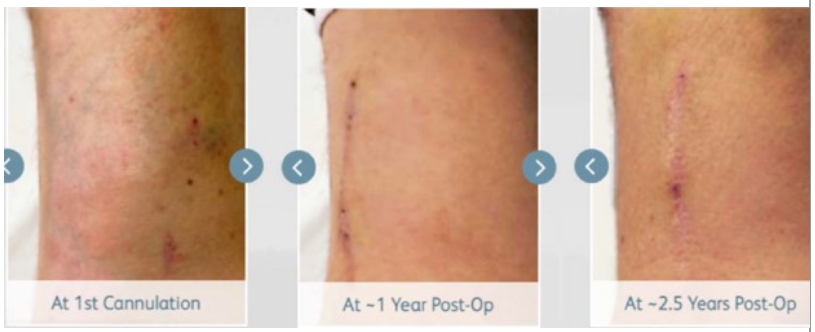
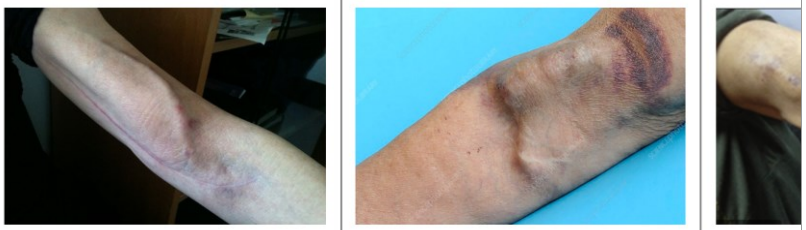


Table 1: Length of follow-up of studies included in the overview

Author, year	Number of subjects	Follow-up
Rajan 2015	33	6 months
Hull 2017	23	1 year
Lok 2017	80	1 year
Radosa 2017	8	6 months
Hull 2018	107	1 year
Mallios 2018	34	mean 141 (range 53-229 days)
Arnold 2019	120	1 year
Berland 2019	32	6 months
Beathard 2020	105	24 months
Hull 2020	60	mean 282±109 (range 103–385) days

			<table><tr><td>Inston 2020</td><td>170</td><td>mean endoAVF group 497 ±187 days; SAVF group 468±148 days</td></tr><tr><td>Mallios 2020</td><td>234</td><td>mean 302 (range 83-873) days</td></tr><tr><td>Shahverdyan 2020</td><td>100</td><td>Median follow up overall 186.5 (range 0-760) days, Ellipsys device 183 (range 1-487), WavelinQ-4F device 185 (range 0-760) days</td></tr><tr><td>Harika 2021</td><td>214</td><td>2 years</td></tr></table> References: 44. Viecelli, A.K., et al., *Vascular Access Outcomes Reported in Maintenance Hemodialysis Trials: A Systematic Review.* American Journal of Kidney Diseases, 2018. **71**(3): p. 382-391.	
14	Consultee 3 BD, manufacturer	**'Validity and generalisability of the studies', Overview, p.36**	In 'Validity and generalisability of the studies', the overview states that 'evidence in the systematic review was mainly from small prospective and retrospective studies.' The committee should note that the Yan Wee review included n=300 patients: the purpose of a systematic review is to aggregate results from a number of small studies in a structured way to provide more robust results. The committee should also note that the evidence reviewed in the overview comprises a total of 1320 patients (Table 1 above), not including two recently published additional studies not referenced in the overview[53,54] and one study (Zemela 2021) listed in the Appendix as not included (see following section). The two additional studies which appear relevant are neither included nor listed in the Appendix as not included report results in an additional n=158 patients (89 endoAVF and 69 SAVF)[53] and n=86 patients (24 endoAVF and 62 SAVF)[54]. Zemela 2021 reports results in a further 35 patients. Evidence reporting results in n=1599 patients is available to	Thank you for your comments. The 'validity and generalizability of the studies' section in the overview only highlights the limitations of the evidence base such as lack of randomised studies. The committee did not state that the evidence for endovascular AVF should be better than surgical AVF. Only evidence on efficacy and safety for endoAVF procedure was assessed in this guidance and most of the evidence included was from observational studies. Therefore, section 1 in the guidance highlighted that ''evidence on its efficacy is limited in quantity and quality' and further research preferably in the form of

			the committee. We submit that the quantity of the available evidence is substantial. References: 53. Shahverdyan, R., et al., *Comparison of Ellipsys Percutaneous and Proximal Forearm Gracz-Type Surgical Arteriovenous Fistulas.* American journal of kidney diseases : the official journal of the National Kidney Foundation, 2021. **01**. 54. Osofsky, R., et al., *Initial Outcomes Following Introduction of Percutaneous Arteriovenous Fistula Program with Comparison to Historical Surgically Created Fistulas.* Annals of Vascular Surgery, 2021.	randomised controlled trials was recommended in 1.6. 2 studies (Shahverdyan 2021, Osofsky 2021) listed by the consultee have been picked up in our update search and have been added to the appendix in the overview. Zemela 2021 is a small case series and is listed in the appendix in the overview.
15	Consultee 3 BD, manufacturer	**'Validity and generalisability of the studies', Overview, p.36**	Stoumpos et al[55] in a large and contemporary UK study concluded that surgical AVF success rates have not improved over time. We submit that it is reasonable to use historical SAVF data as a comparison for the observed efficacy results of endoAVF procedures. References: 55. Stoumpos, S., et al., *A national study of autogenous arteriovenous access use and patency in a contemporary hemodialysis population.* J Vasc Surg, 2019. **69**(6): p. 1889-1898.	Thank you for your comments. The 'validity and generalizability of the studies' section in the overview only highlights the limitations of the evidence base such as lack of RCTs. The committee did not state that the evidence for endovascular AVF should be better than surgical AVF. Only evidence on efficacy and safety for endoAVF procedure was assessed in this guidance and most of the evidence included was from observational studies. Therefore, section 1 in the guidance highlighted that ''evidence on its efficacy is limited in quantity and quality' and further research preferably in the form of randomised controlled trials was recommended in 1.6 to focus on this. 3 studies included in the summary of evidence (in the overview) compared endovascular AVF procedures with historical or retrospective surgical AVF

				data (Arnold 2019; Inston 2020 and Harika 2021).
16	Consultee 3 BD, manufacturer	**Overview, general comment**	The committee should be aware that anecdotally endoAVF has better cosmetic results than SAVF, as a result of less superficial scarring and a less prominent fistula because of lower blood flow (Figure 2 and Figure 3). Figure 2: Example of functional endoAVF created with WavelinQ  Figure 3; Examples of cosmetic appearance of AVF fistula  Delayed creation of vascular access is due in part to patient refusal and is associated with adverse outcomes[56]. Concerns about vascular access are important treatment-related stressors for patients on HD. In a systematic review of 46 studies (n=1034), disfigurement (preserving normal	Thank you for your comments. Section 3.8 in the guidance states that *'the committee was informed in patient commentary that the procedure may have a better aesthetic result than a surgically created fistula'.*

			appearance, visual reminder of disease, and avoiding stigma) was one of six themes identified as significant influences on patient decisions about vascular access[57]. Late referral and delayed creation of vascular access may be due in part to patient refusal and fears of dialysis and also are associated with increased risk of complications[58,59]. Other studies have confirmed appearance and body image as an issue for patients in relation to vascular access[60,61]. The systematic review found that the appearance of an AVF was important determinant of patient refusal to accept HD or consent to an AVF. Patients expressed revulsion when confronted with the sight of a swollen or protruding fistula. Some patients were disturbed by having permanent scars and consequently wanted to avoid having fistulas placed on exposed parts of their limbs. Patients were concerned about the perceptions of others and believed that the appearance of their vascular access attracted unwanted attention and made them feel self-conscious or an outcast. For some people, vascular access was a prevailing symbol of their illness. Patient preference has been reported as an important driver of vascular access[61-64]. Appearance has been identified by patients as a major advantage of catheters[65], which are recognised as being less satisfactory from a clinical point of view. In a study of nephrologists and patients, 80% of nephrologists reported that patient refusal is a major barrier to creating a mature AVF[57]; this study found that 32/48 (68%) patients who were receiving chronic HD using a catheter and were eligible for an AVF had refused it. In formulating its guidance, the committee should be aware of the possibility that endoAVF offers a more acceptable alternative vascular access to patients which may encourage	

			them to accept it at an earlier stage (in the UK in 2018, only 52.8% of patients started dialysis with definitive access[1]). References 56. Casey, J.R., et al., *Patients' perspectives on hemodialysis vascular access: a systematic review of qualitative studies.* Am J Kidney Dis, 2014. **64**(6): p. 937-53. 57. Xi, W., et al., *Who should be referred for a fistula? A survey of nephrologists.* Nephrol Dial Transplant, 2010. **25**(8): p. 2644-51. 58. Oliver, M.J., et al., *Late creation of vascular access for hemodialysis and increased risk of sepsis.* J Am Soc Nephrol, 2004. **15**(7): p. 1936-42. 59. Avorn, J., et al., *Delayed nephrologist referral and inadequate vascular access in patients with advanced chronic kidney failure.* J Clin Epidemiol, 2002. **55**(7): p. 711-6. 60. Quinn, R.R., et al., *The Vascular Access Questionnaire: assessing patient-reported views of vascular access.* J Vasc Access, 2008. **9**(2): p. 122-8. 61. Xi, W., et al., *Patient attitudes towards the arteriovenous fistula: a qualitative study on vascular access decision making.* Nephrol Dial Transplant, 2011. **26**(10): p. 3302-8. 62. Fissell, R.B., et al., *Hemodialysis patient preference for type of vascular access: variation and predictors across countries in the DOPPS.* J Vasc Access, 2013. **14**(3): p. 264-72. 63. Kosa, S.D., C. Bhola, and C.E. Lok, *Measuring patient satisfaction with vascular access: vascular access questionnaire development and reliability testing.* J Vasc Access, 2015. **16**(3): p. 200-5.	

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17	Consultee 3 BD, manufacturer	**Overview, general comment**	EndoAVF is a minimally invasive procedure. It reduces surgical trauma by avoiding skin and soft tissue incision, less need for vessel transposition and manipulation, side branch ligation, and suturing: these are known contributory risk factors to the development of neointimal hyperplasia, an important determinant of delayed maturation[66,67]. Maturation is a significant barrier to optimal RRT: a recent systematic review and meta-analysis of 318 studies (62,712 accesses) reported that mean time to maturation was 3.5 months; only 26% of created fistulas were reported as mature at 6 months[68]. The same review that a prolonged maturation period often requires the use of a bridging catheter[68]. This review found that fistulae placed in incident AVF patients had a longer lifespan than those placed in prevalent AVF patients. A study in Scotland found that failure of AVFs to mature is three times more common (27.2% vs. 9.4%) in prevalent patients[69]. These findings emphasise the need to adopt AV access procedures with short maturation times where possible: as noted above[1] only 52.8% of patients started dialysis with definitive access, in part due to the delay between AV access creation and the need to start HD. The committee should note that although endoAVFs do not mature more quickly than SAVFs, they can typically be cannulated (i.e., become usable) sooner than AVF.	Thank you for your comments. The Committee considered this comment but decided not to change the guidance.

			References: 66. Roy-Chaudhury, P., et al., *Neointimal hyperplasia in early arteriovenous fistula failure.* Am J Kidney Dis, 2007. **50**(5): p. 782-90. 67. Roy-Chaudhury, P., V.P. Sukhatme, and A.K. Cheung, *Hemodialysis vascular access dysfunction: a cellular and molecular viewpoint.* J Am Soc Nephrol, 2006. **17**(4): p. 1112-27. 68. Bylsma, L.C., et al., *Arteriovenous Fistulae for Haemodialysis: A Systematic Review and Meta-analysis of Efficacy and Safety Outcomes.* European Journal of Vascular & Endovascular Surgery, 2017. **54**(4): p. 513-522. 69. Stoumpos, S., et al., *Predictors of sustained arteriovenous access use for haemodialysis.* American Journal of Nephrology, 2014. **39**(6): p. 491-8. 1. NKF-K/DOQI, *National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for hemodialysis adequacy, update 2006.* Am J Kidney Dis, 2006. **48**: p. S2-S90.	
18	Consultee 3 BD, manufacturer	**Overview: general comment**	EndoAVF outcomes are at least equivalent to surgically created brachiocephalic AVF[70,71]. A systematic review and meta-analysis of SAVF patency included 46 papers (n=12,383) and reported a primary failure rate of 23% (95% CI, 18%-28%), a primary patency rate of 60% (95% CI, 56%-64%) at 1 year 51% (95% CI, 44%-58%) at 2 years, and a secondary patency rate of 71% (95% CI, 64%-78%) at 1 year and 64% (95% CI, 56%-73%) at 2 years[15]. The analysis also found a significant decrease in primary patency rate in studies that started recruitment in more recent years. Another systematic review and meta-analysis of 318 studies (62,712 accesses) reported a primary (unassisted) patency rate of 64% at one year, a primary assisted patency rate of 73% at one year, and a secondary patency rate of 79% at one year[68]. 1-year primary patency	Thank you for your comments. References 43 (Lok 2017), 79 (Hull 2018), and 71 (Arnold 2018) are endovascular AVF studies considered in this overview of evidence. All other studies listed here by the consultee are related to surgical AVF (references 15, 17, 68, 70, 72-78, 80-83). The literature search was focused on endovascular AVF and not surgical AVF.

			rates reported elsewhere in the literature range from 55% to 78%[17,72-77], with 1-year secondary patency rates ranging from 54% to 71%[17,72,78]. The committee should note that the reported results of endoAVF in the studies included in the overview compare favourably with the reported SAVF patency rates. The rate of secondary procedures with endoAVF[43,79] has been reported as lower than those reported in the surgical AVF literature[70,80-83]. References: 15. Al-Jaishi, A.A., et al., *Patency rates of the arteriovenous fistula for hemodialysis: a systematic review and meta-analysis.* Am J Kidney Dis, 2014. **63**(3): p. 464-78.70. 16. Yang, S., 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): p. 8-14. 17. Rooijens, P.P., et al., *Radiocephalic wrist arteriovenous fistula for hemodialysis: meta-analysis indicates a high primary failure rate.* Eur J Vasc Endovasc Surg, 2004. **28**(6): p. 583-9. 43. Lok, C.E., et al., *Endovascular Proximal Forearm Arteriovenous Fistula for Hemodialysis Access: Results of the Prospective, Multicenter Novel Endovascular Access Trial (NEAT).* Am J Kidney Dis, 2017. **70**(4): p. 486-497. 68. Bylsma, L.C., et al., *Arteriovenous Fistulae for Haemodialysis: A Systematic Review and Meta-analysis of Efficacy and Safety Outcomes.* European Journal of Vascular & Endovascular Surgery, 2017. **54**(4): p. 513-522. 71. Arnold, R.J.G., et al., *Comparison between Surgical and Endovascular Hemodialysis Arteriovenous Fistula Interventions and Associated Costs.* J Vasc Interv	

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