National Institute for Health and Care Excellence

IP1887 Middle meningeal artery embolisation for chronic subdural haematomas

IPAC date: 11 May 2023

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			Comments on the lay description	
1	Consultee 4 NHS Professional	Lay description	Can be particles, or other embolic material including liquid embolic, or coils.	Thank you for your comment. 'particles' has been replaced by 'embolic agents'. This description is available in 'information for the public'.
2	Consultee 4 NHS Professional	Lay description	Can also be used as an adjunct to surgery to reduce the risk of recurrence	Thank you for your comment. Extra wording has been added, please see 'information for the public'.
3	Consultee 6	Lay description	Not only particles can be used but also liquid embolic agents and coils.	Thank you for your comment. 'particles' has been changed to 'embolic agents'. This description is available in 'information for the public'.
4	Consultee 8 NHS Professional	Lay description	There is an error in the initial description, which mentions particles, where as later in the document other forms of embolisation are also mentioned, which is correct.	Thank you for your comment. 'particles' has been changed to 'embolic agents'. This description is available in 'information for the public'.
			Comments on the main recommendation and highlighting ongoing trials	
5	Consultee 1 United Kingdom Neurointerventional Group	1.1	We disagree with this statement. Although it is accepted that randomised evidence is not available currently, the body of available observational evidence suggests that the treatment is safe with low risk profile and is effective in reducing rates of recurrence or need for surgery depending on mode of use. Randomised evidence will be available in a matter of months, so it seems premature to release guidance at this stage.	Thank you for your comment. The committee makes recommendations based on the assessment of published, peer-reviewed evidence on the safety and efficacy of individual procedures. The committee has considered this comment but decided not to change the 'research'

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			UK evidence is available (doi: 10.1080/02688697.2022.2097200). The use as an adjuvant therapy has not been fully considered. Most of the panel comments were considering this therapy as an alternative to surgery, whereas there is a significant volume of published evidence describing MMAE as an excellent therapy to prevent or treat recurrence either after or in addition to surgery - we urge NICE to consider this treatment paradigm. Having first hand experience working in NICE panels in the past we feel that the current evidence base is sufficient to produce guidance suggesting that MMAE should be CONSIDERED in selected cases after multidisciplinary discussion.	recommendation. The rationale can be found in 'why the committee made these recommendations'. The committee was aware of multiple ongoing RCTs when making the decision, and a new section of the final guidance (3.9) has been added to highlight that the committee was aware of the ongoing research and that the guidance will be reviewed when new evidence is published. Mohamed (2022) - the UK evidence - was included in the appendix. In terms of using this procedure as an adjuvant therapy, this guidance covers the procedure being used at different treatment stages and with different aims, as stated in 'why the committee made these recommendations'. In addition, the overview describes that MMAE can be used to treat primary or recurrent CSDHs, and when combining with surgical evacuation, MMAE can also be applied to prevent the recurrence of CSDHs.
6	Consultee 1 United Kingdom Neurointerventional Group	1.2	Currently 12 multicentre RCTs are recruiting in North America, Europe and Asia. They are years into recruitment, and it is very difficult for UK centres to join these trials at this stage. Funding for an additional UK trial (when so many others are up and running) and the lead time to get this off the ground would result in it being almost impossible to start a UK trial at this stage. Therefore, the NICE guidance is effectively advising against the use of this procedure in clinical practice for the foreseeable future,	Thank you for your comment. Section 1.2 has been changed to "Further research should ideally be randomised controlled trials **or other suitably designed studies. It should** report details of patient selection, technique used, rebleeding, functional outcomes, need for reintervention and length of hospital stay. **Further**

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			or at least undermining support for clinicians when offering MMAE to patients. This may have a significant impact on individual patients who have, for example suffered failed neurosurgical procedures (which may happen in up to 30%). These often frail and elderly patients may then be treated with additional surgery which again is unproven and to our knowledge not NICE approved. These cases are associated with the highest morbidity and mortality currently and therefore MMAE represents a sensible low risk, minimally invasive alternative option for treatment. We advise NICE to suggest that (rather than stating for use in RCTs only) patients be entered into a UK registry that could facilitate treatment based on an MDT discussion and enhanced consent. Without this NICE is effectively asking us to withdraw a service that we currently offer and that has benefitted many patients in the UK since 2019.	**research could also include analysis of registry data for long-term outcomes**." The guidance does not specifically require UK-based RCTs. The committee makes recommendations based on the assessment of published, peer-reviewed evidence on the safety and efficacy of individual procedures. The committee has considered this comment but decided not to change the 'research' recommendation. The rationale can be found in 'why the committee made these recommendations'. Please also see response in comment 17.
7	Consultee 2 NHS professional	1	There is a great deal of evidence that MMA embolisation of CSDH is effective and safe. It would be prudent to consider the stance of this procedure when ongoing RCTs report their results. Given what we know thus far, MMA embolisation should be offered to selected patients with CSDH in neuroscience centres with a interventional neuroradiology service, following multidisciplinary consensus discussion between neurosurgery, neuro radiology and anaesthetics/critical care. Centers performing these procedures should audit their results.	Thank you for your comment. The committee makes recommendations based on the assessment of published, peer-reviewed evidence on the safety and efficacy of individual procedures. The committee has considered this comment but decided not to change the 'research' recommendation. The rationale can be found in 'why the committee made these recommendations'.
8	Consultee 2 NHS professional	1.2	These are running. Preliminary data indicates a benefit of MMA embolisation (personal communication Dr. Nestor Gonzalez; Neurosurgeon, Cedars Sinai Medical Center, L.A, November 2022)	Thank you for your comment. The evidence from personal communication does not meet the inclusion criteria.

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				Section 3.9 has been added to acknowledge the ongoing studies.
9	Consultee 3 Society of British Neurological Surgeons (SBNS)	1	The Society of British Neurological Surgeons (SBNS) is in agreement with the recommendation in the draft Guideline indicating that the intervention should be performed within a research protocol only. CSDH is a high volume condition in neurosurgical practice and the decision will affect the management of a large number of patients. The intervention will need to performed by trained Interventional radiologists who are currently also performing stroke thrombectomy and coiling of aneurysms. The indications for standard neurosurgery procedures for CSDH are well defined and based on good quality evidence. The evidence available is not adequate to define the indications for the use of Middle Meningeal Artery Embolisation (MMAE). The evidence does not clarify if MMAE is better than standard neurosurgical intervention. It is very unlikely to replace standard surgical decompression. The evidence for the role of MMAE in reducing progression or recurrence is also not adequate. There are 11 RCT's that are underway at present and the SBNS is of the view that we should await the outcome of these trials. Professor [redacted] SBNS NICE Co-ordinator	Thank you for your comment.
10	Consultee 4 NHS Professional	1.2	There are multiple randomised controlled trials ongoing at present, due to report shortly. I would recommend holding the publication of guidance until the trial outcomes are reported.	Thank you for your comment. IPAC was aware of multiple ongoing RCTs when making the decision, and section 3.9 has been added.
11	Consultee 4	1.1	This will be depriving some patients of a useful adjunct when surgery may be of high risk to them (or multiple surgeries may be	Thank you for your comment.

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	NHS Professional		of higher risk) - such as a need to be on therapeutic anticoagulation for a metallic heart valve or pulmonary emboli. I think in patients such as this, or those where there is recurrence MMA embolisation should be able to be used as current practice (with multiple publications showing level 2 evidence) whilst we await level 1 evidence.	The committee makes recommendations based on the assessment of published, peer-reviewed evidence on the safety and efficacy of individual procedures. The committee has considered this comment but decided not to change the 'research' recommendation. The rationale can be found in 'why the committee made these recommendations'. Please also see response in comment 17.
12	Consultee 5 Medtronic Ltd	1	Medtronic thank NICE for the opportunity to respond to the draft recommendations for the Interventional Procedure Guideline for Middle Meningeal Embolisation for Chronic Subdural Haematomas (CSDH)(IP1887) We are concerned that the draft recommendation, stipulating that middle meningeal artery embolisation for chronic subdural haematomas should be used 'only in research'. The committee concluded that the evidence did not raise any safety concerns, but there is uncertainty about the efficacy of the procedure. We acknowledge that there are a small number of patients currently being treated, however this research recommendation will prevent access for patients. Feedback from some interventional neuroradiologists is that a UK randomised controlled trial (RCT) would be difficult to do in this population. The committee found no safety concerns and the efficacy in haematoma resolution and reduction was shown for this procedure as discussed in page 16 of the overview document. Therefore, we suggest that this would support 'special arrangements' rather than 'only in research'.	Thank you for your comment. The committee has considered this comment but decided not to change the 'research' recommendation. The rationale can be found in 'why the committee made these recommendations'. Section 1.2 has been changed and the guidance does not specifically require UK-based RCTs.
13	Consultee 7	1	I hope the recommendations suggested is changed from research to selected clinical cases and robust data collection is	Thank you for your comment.

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			maintained. We should be waiting till RCT is done. Its unfair on patients effectively denying patients a relatively safe procedure and avoiding major surgery. There are many treatments that dont have RCT and are standard of care and MMAE has ongoing RCT in place in US. In the meantime we should be able to deliver this safe cost effective procedure that will save NHS millions. We already have the manpower and infrastucture to underatke this procedure. Its all unfounded reasoning that [redacted] has given and should be discounted. MMAE will save lives and money to NHS	The committee makes recommendations based on the assessment of published, peer-reviewed evidence on the safety and efficacy of individual procedures. The committee has considered this comment but decided not to change the 'research' recommendation. The rationale can be found in 'why the committee made these recommendations'. Section 3.9 has been added. Professional expert opinions provide contextual information. The committee considered all professional expert questionnaires alongside other evidence included in the overview in their deliberations.
14	Consultee 7	1.1	I strongly disagree. there are significant benefits of the treatment in selected population. This will save NHS huge money. The neurourgeon Adel's opinion is biased and misguided and will lead to unfortunate harm to patients. I accept we may need mores research and randomised trials to show efficacy but in the meantime we should not deny patients MMAE if needed. I disagree it should be done ONLY in research. The neurourgeon Adel has no experience in this treatment and his opinion should be disregarded as he is only seeing his own benefit and not the benefit this treatment will bring to patient care. I am shocked at the comments he has made that are completely unjustified and lead to injustice to patients.	Thank you for your comment. Please see response in comment 13.
15	Consultee 7	1.2	I accept we need more studies but there are already RCT ongoing.	Thank you for your comment. IPAC was aware of multiple ongoing RCTs

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				when making the decision and section 3.9 has been added.
16	Consultee 7	1	all evidence even if not level 1 shows benefits. In US this has become a standard of care. With due respects Mr Adel opinion is flawed and unjustifed. I accept needs more research and we can continue to gather that but as suggested that this is expensive is incorrect. this traetment will save NHS money and beds. I am a member of UKNG and BSNR	Thank you for your comment. Please see responses in comments 13 and 15.
17	Consultee 8 NHS Professional	1	While the practice has been limited in the UK it is far more widely used in the US and Europe. I understand the evidence is limited and that there are a number of on-going trials at this time, which are going to take a couple of years at least to report. I would not be in favour of wholesale use for all patients with CSDH, however feel it would be appropriate, as someone who does the procedure, to have a remit to perform in patients who are on anticoagulation, have recurrent collections or are not suitable for surgery for some reason. Our practice has been for the above indications, on discussion with our Neurosurgical colleagues with excellent results. I feel the recommendation of "only in a research trial" is a step back from where we currently are and that a better position would be: for consideration in selected case following MDT discussion.	Thank you for your comment. The committee makes recommendations based on the assessment of published, peer-reviewed evidence on the safety and efficacy of individual procedures. The committee has considered this comment but decided not to change the 'research' recommendation. The rationale can be found in 'why the committee made these recommendations'. In terms of some patients who might benefit from this procedure, section 3.5 states "This procedure is not currently a treatment for subdural haematoma with mass effect, but it might have a role in preventing recurrence or progression of haematomas." And section 3.6 states "The committee was informed that this procedure might have a role for people who need to continue taking anticoagulant medication and antiplatelet agents. People

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				on anticoagulants might be at higher risk of chronic subdural haematoma." The committee was aware of multiple ongoing RCTs when making the decision and section 3.9 has been added.
18	Consultee 9 Cambridge University Hospital	1	There are currently a number of randomised controlled studies in process, which are scheduled to report later in this year. It seems premature to issue this guidance prior to these studies reporting. In addition, whilst class 1 evidence is generated, there appears to be a role for MMA embolisation in special cases - for example where there has been a recurrence despite surgical treatment, or the patient requires early restarting of anticoagulation or antiplatelet therapy. Surgical treatment of chronic subdural haematoma is associated with considerable morbidity, as is evidenced by a large proportion of patients being presented at neurosurgical morbidity meetings due to readmission, infection etc.	Thank you for your comment. please see response in comment 17.
			Comments on the procedure description	
19	Consultee 4 NHS Professional	2.4	Depending on the collaterals, MMA embolisation may not be offered after the initial angiography. E.g. with MMA arising from the opthalmic artery, where embolisation would risk retinal blindness	Thank you for your comment. Section 2.4 has been changed to "... If there are significant collateral vessels, **MMA embolisation may not be offered. If the procedure is offered, the collateral vessels** are either occluded using coils before embolisation, or the microcatheter is advanced more distally to avoid them... "
20	Consultee 4	2.5	As well as reduce risk of recurrence	Thank you for your comment.

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	NHS Professional			Section 2.5 has been changed to "This procedure aims to eliminate the blood supply from the MMA to the membrane around the haematoma, to allow the eventual spontaneous resolution of the haematoma **and to reduce the risk of recurrence**."
			Comments on the evidence (overview)	
21	Consultee 1 United Kingdom Neurointerventional Group	overview	To summarise the evidence that you have presented: MMAE significantly reduces the rate of subdural haematoma recurrence and subdural volume at follow up with short hospital stay and low procedural risk of complications. Additionally, Jumah et al (meta-analysis) Efficacy and safety of middle meningeal artery embolization in the management of refractory or chronic subdural hematomas: a systematic review and meta-analysis. Acta Neurochir (Wien). 2020 Mar;162(3):499-507. : 26% lower risk of hematoma recurrence in MMAE and 20% reduction in the need for surgical rescue. This is at variance with the comments of the panel - we are unable to understand the conclusions drawn when the current evidence is saying something completely different - we feel it would be worth co-opting additional expertise. The evidence is not randomised but the results of RCTs will be available in months - it seems premature to release any guidance at this stage. It is stated that this practice does not apply to UK populations: there is a prospective study by Mohamed S in B J Neurosurg. doi: 10.1080/02688697.2022.2097200. documenting use in an English centre. In our experience (this procedure has been performed across the country since 2019), MMAE is very beneficial to patients after	Thank you for your comment. Jumah (2020) and Mohamed (2022) were included in the appendix. IPAC was aware of multiple ongoing RCTs when making the decision and section 3.9 has been added. In the main evidence, 9 articles were included, when reported, none of the studies were carried out in the UK. So, there was no data relevant to the UK context. Based on the current evidence, the overview describes "MMAE was used to treat primary or recurrent CSDHs, and when combining with surgical evacuation, MMAE was also applied to prevent the recurrence of CSDHs. Therefore, MMAE has been done in 3 treatment stages: • upfront or primary embolisation in patients with a previously untreated CSDH so embolisation was used as the first treatment without concomitant surgical intervention.

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			failed surgery (which may occur up to 30% of the time) either as a stand-alone therapy or in conjunction with neurosurgery. Additionally, it is very useful for high-risk populations (those on anti-thrombotic therapy). Having this procedure available as an option after failed surgery (with its low risk profile) allows the multi-disciplinary team to consider this treatment as an adjuvant or bail-out therapy. This allows treatment of patients with refractory subdural collections that are associated with the most severe morbidity and high mortality. In the absence of MMAE the patients are likely to be subjected to the currently unproven practice of repeat neurosurgery, remembering that these patients are often frail and elderly. We urge the NICE team to consider this patient group specifically. Additionally, we suggest that the NICE team present the evidence clearly/separately for MMAE as an adjuvant therapy.	• prophylactic or adjunct embolisation after surgical evacuation without evidence of interval postoperative CSDH recurrence (surgery and embolisation usually within 7 days). • rescue embolisation for recurrent CSDH after previous surgical evacuation (more than 7 days after primary surgery). Of the 9 studies, 3 studies presented the outcome data for different treatment purposes separately (Ironside 2021; Haldrup 2020; Nia 2022), 1 study focused on different embolic agents in each treatment stage (Scoville 2022), and 3 studies (Dicpinigaitis 2021; Catapano 2021; Khorasanizadeh 2022) reported the outcomes of MMAE used in different treatment stages as a whole. Where possible, the outcomes for MMAE used in specific treatment stage will be described separately." Therefore, the evidence for MMAE as an adjuvant therapy has been presented separately where possible. Please see responses in comments 5 and 17.
22	Consultee 6	overview	Please also consider Henry 2022 (https://pubmed.ncbi.nlm.nih.gov/36170165/) meta-analysis. and Sam Ng 2020 (https://pubmed.ncbi.nlm.nih.gov/31862830/) randomised controlled trial There are 14 randomised studies underway	Thank you for your comment. Ng (2020) was included in the main evidence (in systematic reviews) and appendix. Henry (2022) has been added to the appendix, and 4 ongoing trials have been included in the overview:

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			(https://clinicaltrials.gov/ct2/results?cond=Chronic+Subdural+Hematoma&term=embolisation&cntry=&state=&city=&dist=)	NCT04574843, NCT04095819, NCT05374681, NCT04816591
23	Consultee 6	overview	Please see Saffwan Mohamed, Alvaro Villabona, Oliver Kennion, Rajeev Padmananbhan, Aslam Siddiqui, Shahid Khan, Manjunath Prasad & Nitin Mukerji (2022): Middle meningeal artery embolisation for chronic subdural haematomas: the first prospective UK study, British Journal of Neurosurgery, DOI: 10.1080/02688697.2022.2097200	Thank you for your comment. Mohamed (2022) was included in the appendix.
24	Consultee 6	overview	This is not true: see Sam Ng 2020 (https://pubmed.ncbi.nlm.nih.gov/31862830/) randomised controlled trial	Thank you for your comment. Ng (2020) was included in the main evidence (in systematic reviews) and appendix. Extra text has been added to the overview to reflect this pilot randomised study.
			Comments on patient involvement	
25	Consultee 5 Medtronic Ltd	3.4	Medtronic acknowledge that no patient commentary was provided in response to this interventional procedural guidance. Medtronic believe that the inclusion of the patient voice is essential as it demonstrates active steps to improve the healthcare service provisions by improving patient satisfaction, healthcare outcomes and most importantly reducing health inequalities and inequities.	Thank you for your comment. NICE sent a questionnaire to relevant patient organisations but none was returned.
26	Consultee 7	3.4	this should be sought actively and surely many patients will come forward	Thank you for your comment. NICE sent a questionnaire to relevant patient organisations but none was returned.
			Comments relating to the target patients who might benefit from this procedure	

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27	Consultee 1 United Kingdom Neurointerventional Group	3.5	This is a matter of opinion only and "mass effect" needs to be defined before making this statement, and then this needs to be backed up by evidence. There are observational studies showing that MMAE can be used to treat subdural haematomas with midline shift: Gomez-Paz S, et al. Upfront middle meningeal artery embolization for treatment of chronic subdural hematomas in patients with or without midline shift Interv Neuroradiol. 2021 Aug; 27(4): 571–576.	Thank you for your comment. Section 3.5 has been changed to "This procedure is not **currently** a treatment for subdual haematoma with mass effect, but it might have a role in preventing recurrence or progression of haematomas." Gomez-Paz et al. (2021) was included in the appendix.
28	Consultee 1 United Kingdom Neurointerventional Group	3.6	Agree - in our experience MMAE aids treatment in this population.	Thank you for your comment.
29	Consultee 1 United Kingdom Neurointerventional Group	3.9	This does not mean that this therapy is not useful in patients who have symptomatic lesions. Many studies include only only symptomatic lesions and this is compatible with UK-wide experience. Furthermore, the current evidence base suggests that MMAE reduces recurrence if used in addition to surgery and reduces the need for surgery if being used as an up-front treatment. We also urge NICE to consider use for those with failed surgery which may occur in up to 30% of cases. Currently there is no proven therapy for these patients.	Thank you for your comment. This guidance covers the procedure being used at different treatment stages and with different aims, as stated in 'why the committee made these recommendations'. In addition, the overview describes that MMAE can be used to treat primary or recurrent CSDHs, and when combining with surgical evacuation, MMAE can also be applied to prevent the recurrence of CSDHs. Please see responses in comments 5 and 17.
30	Consultee 2 NHS professional	3.9	The role of MMA embolisation in CSDH will become clearer as experience grows (there are currently a multitude of RCT's running). It is clear that embolisation cannot be performed alone in patients with significant neurologic symptoms from mass effect - these	Thank you for your comment. The committee was aware of multiple ongoing trials and will review the guidance when new evidence is published.

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			patients must have their haematomas surgically drained. The major role of embolisation is likely to be adjunctive, in preventing recurrence following surgery (which occurs in up to 30% of patients). Patients at increase risk of recurrence (such as those with CT imaging features of "membranes" within the haematoma, and patients taking anticoagulants) also benefit from MMA embolisation. In asymptomatic patients with large CSDHs, there may also be a role for embolisation (although this is less clear)	This guidance covers the procedure being used at different treatment stages and with different aims, as stated in 'why the committee made these recommendations'. In addition, the overview describes that MMAE can be used to treat primary or recurrent CSDHs, and when combining with surgical evacuation, MMAE can also be applied to prevent the recurrence of CSDHs. Please also see response in comment 17.
31	Consultee 5 Medtronic Ltd	3.5	The committee highlighted that middle meningeal embolisation is not a procedure for subdural haematoma with mass effect. However, several studies cited in the draft IPG overview have reported reduction in mass of the haematoma (Catapano 2021; Scoville 2022). A paper by Nia et al., 2022 showed significantly shorter hospital stay, which would lead to a reduction in treatment costs, and increase patient satisfaction. Nia et al., 2022 also illustrated a lower chance of treatment failure when embolisation is compared to surgery as primary treatment. We understand that patients with severe symptoms, cannot wait for embolisation to take effect, as the haematoma reduction would not occur immediately. However, a combination of surgical resection and then preventative embolisation (to prevent recurrence) could provide a valuable option. There are relatively high recurrence rates for patients treated with surgery (~20% in 1 year) embolisation would be useful preventative treatment as it would avoid multiple surgeries. Embolisation would be a beneficial alterative for patients who are currently asymptomatic, but have a hematoma increasing in size. The procedure would stop the growth and size of the haematoma, without the added risks of open brain surgery. Ideally, CSDH should be treated in a similar way as we see now in centres specializing in AVM treatment, which would involve a combined	Thank you for your comment. section 3.5 has been changed to "This procedure is not **currently** a treatment for subdual haematoma with mass effect, but it might have a role in preventing recurrence or progression of haematomas." This guidance covers the procedure being used at different treatment stages and with different aims, as stated in 'why the committee made these recommendations'. In addition, the overview describes that MMAE can be used to treat primary or recurrent CSDHs, and when combining with surgical evacuation, MMAE can also be applied to prevent the recurrence of CSDHs. Please also see response in comment 17. Catapano et al. (2021), Nia (2022) and Scoville (2022) were included in the main evidence.

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			team of neurosurgeons and interventional neuroradiologists to decide on a patient per patient basis which treatment, or combination of treatments would be the best option for this specific patient. One treatment should not exclude the other, but having either option or a combination of both helps achieve the best outcome for the patient. We kindly ask the committee to amend the wording to say that this procedure could be an option for subdural haematoma following the advice of the neurosurgeons an international neuroradiologists. References: • Catapano, J.S. et al. (2021) “Radiographic clearance of chronic subdural hematomas after middle meningeal artery embolization,” Journal of NeuroInterventional Surgery [Preprint]. Available at: https://doi.org/10.1136/neurintsurg-2021-018073. • Nia, A.M. et al. (2022) “Trends and outcomes of primary, rescue, and adjunct middle meningeal artery embolization for chronic subdural hematomas,” World Neurosurgery, 164. Available at: https://doi.org/10.1016/j.wneu.2022.05.011. • Scoville, J.P. et al. (2022) “Radiographic and clinical outcomes with particle or liquid embolic agents for middle meningeal artery embolization of nonacute subdural hematomas,” Interventional Neuroradiology, p. 159101992211046. Available at: https://doi.org/10.1177/15910199221104631.	
32	Consultee 5 Medtronic Ltd	3.9	We agree that if the patient is completely asymptomatic, and the hematoma does not increase in size, treatment may not be required. However, an asymptomatic patient with a growing haematoma, may need treatment in the future. Early treatment with embolisation, is less invasive reducing hospital stay and increase patient quality of life. For patients who previously have had surgery, and a haematoma reoccurs, embolisation may be a good option for early treatment as opposed to waiting for the	Thank you for your comment. This guidance covers the procedure being used at different treatment stages and with different aims, as stated in ‘why the committee made these recommendations’. In addition, the overview describes that MMAE can be used to treat primary or recurrent CSDHs, and when combining with

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			patient to become symptomatic again, and to prevent any subsequent haematomas from occurring.	surgical evacuation, MMAE can also be applied to prevent the recurrence of CSDHs. Please also see response in comment 17.
33	Consultee 7	3.9	not necessary true.	Thank you for your comment. Please see response in comment 29.
			Comments relating to embolic agents	
34	Consultee 1 United Kingdom Neurointerventional Group	3.7	This does not mean that the procedure is not effective. It could equally suggest that similar results can be achieved with different embolic agents.	Thank you for your comment. Section 3.7 specifies that the uncertainty remains in which embolic agent is most effective.
35	Consultee 1 United Kingdom Neurointerventional Group	3.8	There is no evidence to support this and at most this will be exceptionally rare - we feel it does not deserve a comment in the NICE document - we suggest that this is removed. There are multiple studies describing the risks/complications of MMAE and this is not a feature described. MMAE has been performed in conjunction with surgery for a number of years and this has not been encountered. Endovascular treatment with liquid embolic agents have been used in conjunction with open neurosurgery for many years, for example in combined brain and spinal arteriovenous malformation treatment. What is more important is that recurrence rates after surgery occur in 10-30% and that an effective minimally invasive treatment or adjuvant treatment is needed for these patients.	Thank you for your comment. Section 3.8 has been removed.

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36	Consultee 2 NHS professional	3.7	The question of which embolic agent is most effective remains to be answered. However the growing evidence indicates that any embolisation reduces recurrence and retards CSDH growth	Thank you for your comment. Please see response in comment 34.
37	Consultee 2 NHS professional	3.8	The embolic agents used in MMA embolisation are identical to those used in other neurointerventional procedures. This includes vascular malformations of the brain. Combined embolisation and surgical treatment of brain AVMs, for example, is routinely performed in specialised units (neuroscience centres that would be performing procedures like MMA embolisation). Diathermy in embolised brain AVMs has (to my knowledge) never resulted in an adverse outcome. For context it is important to note that: - The arteries embolised (middle meningeal arteries) are outside the brain. - The volume of embolic agent used in MMA embolisation is invariably less that that used in vascular malformation embolisation. -Because of the low volume of embolic agent used, the artefacts on imaging are negligible (having reported on studies of patients who have undergone MMA embolisation)	Thank you for your comment. Section 3.8 of the draft guidance has been removed for the final guidance.
38	Consultee 4 NHS Professional	3.8	The volume of embolic material used is low. The artefacts as a result are minimal and in no way comparable to artefacts seen from embolic material in other neurointerventional procedures (e.g. dural AV fistula embolisation).	Thank you for your comment. Section 3.8 of the draft guidance has been removed for the final guidance.
39	Consultee 5 Medtronic Ltd	3.8	The committee mentioned that certain embolisation agents may cause sparks. A combined search of Pubmed and Embase gave a total of four single case reports (Hira 2011, Mull 2012, Schirmer 2006 and Smith 2009) of sparking, with the latest case report published in 2012. All occurred when mono-polar diathermy was used. This is a known artifact with Tantalum, which is why our IFU contains the following warning: "Due to the possibility of electrical arcing with the tantalum metal in the Onyx™ LES material, use of	Thank you for your comment. Section 3.8 of the draft guidance has been removed for the final guidance. Hira (2011), Ierardi (2018), Ne (2018), Smith (2009), Schirmer (2006), Mull (2012) - did not meet the inclusion criteria.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
			monopolar electrocautery devices for surgical resection of brain arteriovenous malformations (bAVMs) or arteriovenous fistula embolized with Onyx™ LES should be avoided. Bipolar devices should be used with caution." The caution with bipolar diathermy means that resection should be done next to the Onyx cast and not through it. As mentioned by one clinician, as it is black, this assists in identifying the location where to resect. Since 2012, more than 500.000 (please mark this figure as commercial in confidence [CIC]) vials of Onyx have been sold, without the issue having reoccurred. Physician training on the product has had great effects in preventing this from happening. The CT artifacts are indeed known to occur with tantalum. However, these are not seen with MRI, and are present to a lesser extent than with coils (Ierardi 2018, Né 2018) We kindly ask the committee to amend the wording to say that liquid embolic agents with a metallic component may have the risk of sparking when electrocautery devices are in direct contact with the liquid embolic agent. References: • Hira A, Chao K. Direct Endoscopic Intratumoral Injection of Onyx for the Preoperative Embolization of a Recurrent Juvenile Nasal Angiofibroma. Interventional Neuroradiology. 2011;17(4):477-481. doi:10.1177/159101991101700413 • Ierardi, A.M. et al. (2018) “Onyx liquid embolic system (LES): An underestimated tool in the management of peripheral bleedings,” Journal of Endovascular Resuscitation and Trauma Management, 2(2). Available at: https://doi.org/10.26676/jevtm.v2i2.46. • Né, R. et al. (2018) “Embolization with ethylene vinyl alcohol copolymer (Onyx®) for peripheral hemostatic and non-hemostatic applications: A feasibility and safety study,” Quantitative Imaging in Medicine and Surgery, 8(3), pp. 280–290. Available at: https://doi.org/10.21037/qims.2018.04.03. • Smith, S. J., A. Thomas, and R. D. Ashpole. "Intra-operative	

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
			combustion of Onyx embolic material." British Journal of Neurosurgery 23.1 (2009): 76-78. • Schirmer, Clemens M., Vasilios Zerris, and Adel M. Malek. "Electrocautery-induced ignition of spark showers and self-sustained combustion of onyx ethylene-vinyl alcohol copolymer." Operative Neurosurgery 59.suppl_4 (2006): ONS-E413. • Mull, Aaron, et al. "A cautionary report: Creation of intraoperative sparks and embers from Onyx embolic material during surgical resection of arteriovenous malformations." Plastic and Reconstructive Surgery 129.2 (2012): 401e-402e.	
40	Consultee 7	3.7	agree but all these seem to show the benefits of the treatment.	Thank you for your comment. Please see response in comment 34.
41	Consultee 7	3.8	this is possible but not common and shouldn't be the reason to deny pts MMAE	Thank you for your comment. Section 3.8 of the draft guidance has been removed for the final guidance.
			Comments relating on PEQs	
42	Consultee 6	PEQs	Unfortunately [redacted] failed to appreciate the role of this procedure in the UK/NHS is not for asymptomatic patients, but for those were surgery failed and those with co-morbidities with need of anti thrombotic agents. He also failed to understand this procedure doesn't requires extra training for the INR as this is a procedure routinely performed for other indications and t can be performed under local anaesthesia. There was an imbalance in the number of neurosurgeons (3) expert versus INR (1) experts. There is a conflict of interest of neurosurgeons not wanting to 'loose' another type of procedure for the INR. The committee should have been more balanced.	Thank you for your comment. Professional expert opinions provide contextual information. The committee considered all professional expert questionnaires alongside other evidence included in the overview in their deliberations.
43	Consultee 6	link to PEQs	This is not available	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
				This has been fixed.

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."