HAUTE AUTORITÉ DE SANTÉ

APPENDIX TO TECHNOLOGICAL ASSESSMENT REPORT

Organisation of the early management of acute ischaemic stroke using mechanical thrombectomy

July 2018

This appendix to the technological assessment report can be downloaded from
www.has-sante.fr

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This document was approved by the College of the French National Authority for Health in July 2018.

Contents

Appendix 1. Documentary search

Automated bibliographic databases

- *Medline (National Library of Medicine, United States);*
- *The Cochrane Library (Wiley Interscience, United States);*
- BDSP Public Health Database;
- Science Direct (Elsevier);
- *National Guideline Clearinghouse (Agency for Healthcare Research and Quality, United States);*
- *HTA Database (International Network of Agencies for Health Technology Assessment).*

Table 1. Documentary search strategy

Study type / Topic / Terms used		**Search period**	**Number of references**
Guidelines			
Stage 1	"Thrombolytic Therapy"[Majr] OR "Embolectomy"[Majr:NoExp] OR "Thrombectomy"[Majr] OR embolectomy OR thrombectomy OR retrieval clot OR retrieval device OR retrieval stent OR stent retrievers OR penumbra system OR solitaire stent Or mechanical thrombus removal Or mechanical ambolus OR removal retrievable stent Or mechanical recanalization OR mechanical thrombolysis [title/abstract] AND "Stroke"[Mesh] OR "Hypoxia-Ischemia, Brain"[Mesh] OR "Brain Ischemia"[Mesh] OR "Ischemic Attack, Transient"[Mesh] OR "Brain Infarction"[Mesh] OR "Intracranial Embolism and Thrombosis"[Mesh] OR "Intracranial Embolism"[Mesh] OR stroke OR Brain Infarction Or Cerebral Infarction Or Intracranial Embolism OR Cerebrovascular Accident Or Stroke Or Brain hypoxia Or Brain ischemia OR acute ischemic stroke [title/abstract]	01/2010-10/2017	
AND			
Stage 2	Consensus OR guideline* OR recommend* or guidance [title]		64
Meta-analyses, systematic reviews			
Stage 1		10/2010-10/2017	
AND			
Stage 3	"Meta-Analysis as Topic"[Mesh] OR "Meta-Analysis "[Publication Type] OR "Review Literature as Topic"[Mesh] OR “Meta Analysis” OR “systematic Review” OR “Literature review” Or "Quantitative Review" OR “pooled analysis” Field: Title/Abstract		359
Organisation of care **Management optimisation**			
Stage 1		10/2010-10/2017	
AND			
Stage 3	"Continuity of Patient Care"[Mesh:NoExp] OR "Patient Care Team"[Mesh] OR "Hospital Rapid Response Team"[Mesh] OR "Emergency Medical Services/organization and administration"[Mesh] OR "Emergency Medical Services/standards"[Mesh] Or optimiz* OR team OR staff OR triage [title]		54

Study type / Topic / Terms used		Search period	Number of references
Organisation of care **Telemedicine**			
Stage 1		010/2010-10/2017	
AND			
Stage 3	"Telemedicine"[Mesh] OR telehealth OR telemedicine OR telestroke[title/abstract]		10
Organisation of care **Assessment/Quality of care**			
Stage 1		010/2010-10/2017	
AND			
Stage 4	"Health Care Quality, Access, and Evaluation"[Mesh:NoExp] OR "Quality of Health Care"[Mesh:NoExp]) OR "Quality Indicators, Health Care"[Mesh:NoExp] or accreditation or certification or indicator* or quality [title]		59
Total number of references obtained		**546**	

Bibliographic monitoring was continued on the topic until April 2018.

In addition, the contents of the following journals were analysed throughout the project: Annals of Internal Medicine, Archives of Internal Medicine, British Medical Journal, Canadian Medical Association Journal, JAMA, Lancet, New England Journal of Medicine, Presse Médicale.

The international websites of the relevant societies cited below were searched in addition to systematically queried sources:

Adelaide Health Technology Assessment
Agencia de Evaluación de Tecnología e Investigación Médicas de Cataluña
Agencia de Evaluación de Tecnologías Sanitarias de Galicia
Agency for Healthcare Research and Quality
Agency for Healthcare Research and Quality /National Quality Measures Clearinghouse
Agency for Healthcare Research and Quality /Patient Safety Network
Alberta Heritage Foundation for Medical Research
American College of Physicians
American Medical Association
Australian Government - Department of Health and Ageing
Blue Cross Blue Shield Association - Technology Evaluation Center
Bibliothèque médicale Lemanissier
Canadian Agency for Drugs and Technologies in Health
Centers for Disease Control and Prevention
California Technology Assessment Forum
Centre fédéral d'expertise des soins de santé

CISMeF
CMAInfobase
Collège des Médecins du Québec
Cochrane Library Database
Centre for Review and Dissemination databases
Department of Health (UK)
ECRI Institute
Evaluation des Technologies de Santé pour l'Aide à la Décision
Euroscan
European Stroke Organisation
European Society of Neuroradiology
Fédération Hospitalière de France
GIN (Guidelines International Network)
Haute Autorité de santé
Horizon Scanning
Institute for Clinical Systems Improvement
Institut National d'Excellence en Santé et en Services Sociaux
Instituto de Salud Carlos III / Agencia de Evaluación de Tecnologías Sanitarias
Iowa Healthcare collaborative
National Coordinating Centre for Health Technology Assessment
National Horizon Scanning Centre
National Health and Medical Research Council
National Health committee
National Institute for Health and Clinical Excellence
National Institutes of Health
National Stroke Foundation
New Zealand Guidelines Group
Servicio de Evaluación de Tecnologías Sanitarias OSTEBA
Ontario Health Technology Advisory Committee
Scottish Intercollegiate Guidelines Network
Singapore Ministry of Health
Société Française Neuro-vasculaire
West Midlands Health Technology Assessment Collaboration
World Health Organization

Appendix 2. AGREE II checklist

		ITEM
Scope & purpose	1	The overall objective(s) of the guideline is (are) specifically described
	2	The health question(s) covered by the guideline is (are) specifically described
	3	The population to whom the guideline is meant to apply is specifically described
		score (%)
Stakeholder involvement	4	The guideline development group includes individuals from all the relevant professional groups
	5	The views and preferences of the target population have been sought
	6	The target users of the guideline are clearly defined
		score (%)
Rigour of development	7	Systematic methods were used to search for scientific evidence
	8	The criteria for selecting the evidence are clearly described
	9	The strengths and limitations of the body of evidence are clearly described
	10	The methods for formulating the recommendations are clearly described
	11	The health benefits, side effects and risks have been considered in formulating the recommendations
	12	There is an explicit link between the recommendations and the supporting scientific evidence
	13	The guideline has been externally reviewed by experts prior to its publication
	14	A procedure for updating the guideline is provided
		score (%)
Clarity of presentation	15	The recommendations are specific and unambiguous
	16	The different options for management of the condition or health issue are clearly presented
	17	Key recommendations are easily identifiable
		score (%)
Applicability	18	The guideline describes facilitators and barriers to its application
	19	The guideline provides advice and/or tools on how the recommendations can be put into practice
	20	The potential resource implications of applying the recommendations have been considered
	21	The guideline presents monitoring and/or auditing criteria
		score (%)
Editorial independence	22	The views of the funding bodies have not influenced the content of the guideline
	23	Competing interests of guideline development group members have been recorded and addressed
		score (%)
Overall assessment		Overall quality of the guideline
		Recommendation for use

Appendix 3. AMSTAR checklist

	Questions	Answers
1	**Was an *"a priori" design provided*?** The research question and inclusion criteria should be established before the conduct of the review	Yes No Can't answer Not applicable
2	**Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place	Yes No Can't answer Not applicable
3	**Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialised registers, or experts in the particular field of study, and by reviewing the references in the studies found	Yes No Can't answer Not applicable
4	**Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports, based on their publication status, language, etc.	Yes No Can't answer Not applicable
5	**Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided	Yes No Can't answer Not applicable
6	**Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported	Yes No Can't answer Not applicable
7	**Was the scientific quality of the included studies assessed and documented?** *"A priori"* methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomised, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant	Yes No Can't answer Not applicable
8	**Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigour and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations	Yes No Can't answer Not applicable
9	**Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies	Yes No Can't answer

	Questions	Answers
	were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?)	Not applicable
10	**Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test)	Yes No Can't answer Not applicable
11	**Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies	Yes No Can't answer Not applicable

Appendix 4. INAHTA development and review checklist for health technology assessment reports

Item	yes	partly	no
Preliminary			
1 Appropriate contact details for further information?			
2. Authors identified?			
3. Statement regarding conflict of interest?			
4 Statement on whether report externally reviewed?			
5. Short summary in non-technical language?			
Why?			
6. Reference to the question that is addressed?			
7. Scope of the assessment specified?			
8. Description of the assessed health technology?			
How?			
9. Details on sources of information provided?			
10. Information on selected data for the assessment?			
11. Information on interpretation of the selected data?			
What then?			
12. Findings of the assessment provided?			
13. Findings of the assessment discussed?			
Implications			
14. Conclusions of the assessment provided?			
15. Medico-legal implications stated?			
16. Conclusions of the assessment clearly stated?			
17. Suggestions for further action?			

Appendix 5. Questionnaire addressed to regional health boards

QUESTIONNAIRE SENT TO NATIONAL REFERENCE REGIONAL HEALTH BOARD STEERING COMMITTEE FOR STROKE

"Impact of mechanical thrombectomy on the organisation of the early management of acute ischaemic stroke"

July 2017

Within the scope of its health technology and medical procedure assessment duties, the French National Authority for Health (HAS) is currently assessing the "impact of mechanical thrombectomy on the organisation of the early management of acute ischaemic stroke". This assessment addresses the second part of the assessment of the efficacy and safety of endovascular intracranial artery thrombectomy published on-line last November (http://www.has-sante.fr/portail/jcms/c_2624413/fr/evaluation-de-thrombectomie-des-arteres-intracraniennes-par-voie-endovasculaire-feuille-de-route).

Therefore, the work process adopted by HAS for this second assessment is based on a critical analysis of the literature, and particularly requires the collection of information from the organisations involved in acute ischaemic stroke management. These organisations are consulted as "stakeholders", pursuant to decree No. 2013-413 of 21 May 2013 (available to view at www.legifrance.gouv.fr).

In recent years, the emergence of mechanical thrombectomy (MT) has made it possible to potentially expand management regimens, and improve IS treatment efficacy. In its 2016 technological assessment report on the benefit-risk aspects of MT, HAS considered that the procedure offered a benefit in the management of patients with acute ischaemic stroke, associated with intracranial large vessel occlusion of the anterior circulation, visible on imaging within 6 hours after the onset of symptoms, either from the outset in combination with intravenous (IV) thrombolysis, or as a second-line procedure: after IV thrombolysis treatment failure, or on its own in the event of contraindication to IV thrombolysis.

This activity is performed by interventional neuroradiology units governed by SIOS schemes and the 2007 decrees in relation to establishment and practice. The inclusion of mechanical thrombectomy as a conventional intracranial vascular recanalisation method requires an adjustment of regional organisation in order to select patients and dispatch them as quickly as possible to comprehensive stroke centres equipped with an interventional neuroradiology platform.

In this context, we are seeking a description of the current regional organisation of early stroke management.

Please note that it is necessary to justify your responses, and cite and attach source documents wherever possible.

NEUROVASCULR SERVICES: general organisation

Q1

What is the current regional organisation of early stroke management?

Response:

Q2

What are your analyses of the organisation and challenges in respect of the optimal roll-out of MT on a regional level?

- **Projected growth of MT activity?**
- **Regional network?**
- **Adequacy of human resources to cover daytime activity, on-call service, out-of-hours service and continuity of care?**
- **Has the new organisation factored in the introduction of MT?**

Response:

Q3

Can you describe your feedback on the introduction of MT in stroke management?

Response:

Q4

Can you describe your feedback on the introduction of MT in stroke management?

- **Have you encountered any problems? If so, which?**
- **What is the MT care provision map in your region?**
- **Have you implemented interfacility transfer protocols to enable patients admitted for IV thrombolysis to access the INR technical platform if MT is indicated?**

Response:

REMARKS

R1

Would you like to add any further comments?

Response:

Appendix 6. France-AVC patient association questionnaire and responses

QUESTIONNAIRE SENT TO FRANCE-AVC ASSOCIATION

"Impact of mechanical thrombectomy on the organisation of the early management of acute ischaemic stroke"

July 2017

Within the scope of its health technology and medical procedure assessment duties, the French National Authority for Health (HAS) is currently assessing the "impact of mechanical thrombectomy (MT) on the organisation of the early management of acute ischaemic stroke". This assessment addresses the second part of the assessment of the efficacy and safety of endovascular intracranial artery thrombectomy published on-line last November (http://www.has-sante.fr/portail/jcms/c_2624413/fr/evaluation-de-thrombectomie-des-arteres-intracraniennes-par-voie-endovasculaire-feuille-de-route).

Please note that it is necessary to justify your responses, and cite and attach source documents wherever possible.

You are reminded that this questionnaire and the responses made by all stakeholders will be included in the final HAS report, published on-line on the HAS website.

Due to assessment scheduling constraints, it is necessary that we receive your contributions by **15/09/17** (by e-mail for the following address: (has.seap.secretariat@has-sante.fr).

Public information and consent

Q1

In your view, how well informed is the general public about the early stroke management pathway?

Response:

VERY ILL-INFORMED

Q2

Do you consider that you have access to enough information on early stroke management? 51°

If yes, please provide your information sources (healthcare professionals, patient associations, discussion forums, etc.)?

Otherwise, which type(s) of information would you like to be able to access?

Response:

NO – FRANCE AVC INFORMED, BUT NOT ENOUGH COOPERATION WITH PROFESSIONALS

Q3

In your view, how well informed is the general public about mechanical thrombectomy?

Is the general public also aware of the benefit-risk balance of mechanical thrombectomy?

Is this information comprehensible for the public?

Response:

NOT AT ALL

NO

THE LITTLE INFORMATION IS RELATIVELY CLEAR

Patient/entourage information and consent

Q4

In your view, is the information provided to patients and their entourage clear, faithful, comprehensive and appropriate?

Response:

WHILE INFORMATION IS PROVIDED, IT COULD BE CLEARER-

BUT INFORMATION IN THE ACUTE PHASE IS OFTEN MISUNDERSTOOD AND NOT EASILY ACCEPTED.

Q5

Would the patient and/or his/her entourage like, insofar as possible, a more active role in the early management of stroke, particularly when decisions involving the patient are made?

Response:

SOME PATIENTS

Patient expectations

Q6

Are there any patient expectations and/or requirements in relation to early stroke management in general, and mechanical thrombectomy therapy in particular, in terms of:

- **Regional organisation;**
- **Stroke centre admission and reception of the patient and his/her entourage;**
- **Patient transfer to the INR unit;**
- **Or any other aspect (please specify)?**

Response:

NATURALLY, ALL PATIENTS AND FAMILIES WOULD LIKE THE HIGH-QUALITY CARE TO WHICH THEY FEEL THEY ARE ENTITLED

Q7

Are there any patient expectations and/or requirements in relation to early stroke management using MT, in terms of:

- **Procedural regimens;**
- **Choice of anaesthetic regimen;**
- **Pain management;**
- **Procedural safety;**
- **Or any other aspect (please specify)?**

Response:

IF 10% OF PATIENTS RECEIVE THROMBOLYSIS AND IN SOME CASES THROMBECTOMY – DO YOU THINK THAT THE REMAINING 90% ARE SATISFIED AND HAVE NO EXPECTATIONS?

Other aspects

Q8

Are there any finalised or ongoing discussions in your association in respect of the stroke management pathway? If yes, what is the outcome?

Response:

YES – IMPROVES COOPORATION WITH STROKE CENTRE LEADERS

Q9

Would you like to add any further comments?

Response:

IT IS WORTHWHILE CONTINUING THE IMPETUS SET IN MOTION BY THE STROKE PLAN

Appendix 7. Assessment report review questionnaire addressed to the "Mechanical thrombectomy in the management of cerebral infarction patients" Steering Committee ("COPIL DGOS")

REVIEW OF THE DRAFT CONFIDENTIAL DOCUMENT ENTITLED

"Assessment of the impact of mechanical thrombectomy on the organisation of the early management of acute ischaemic stroke"

February 2018

Thank you for accepting to take part in this assessment, and for taking the time to review our assessment report and respond to this questionnaire.

We would be grateful if you could justify any remarks and suggestions you may have to allow us to envisage any amendments required. Please also provide the most accurate reference possible to any relevant publications that have not been taken into consideration and which, in your view, would meet the selection criteria applied.

Your responses will be featured in full in the definitive assessment report published by HAS following its assessment process. Hence, until that time, the justification document that you have been sent remains strictly confidential.

Due to assessment scheduling constraints, it is necessary that you return your response to us by e-mail by **13 March 2018** (has.seap.secretariat@has-sante.fr). After that deadline, we will consider that you have no observations to make, and will deem your failure to respond as tacit approval of our draft justification.

Pending the opportunity to enhance this report further with your review, we remain entirely at your disposal should you require any further details.

CONTENT OF ASSESSMENT

C1 **In your view, are the assessment questions and areas explicit and relevant?**

Response:

C2 **In your view, are the documentary searches and selections carried out transparent and appropriate for the assessment scope in question (see appendix 1)?**

Response:

C3 **Are you aware of any relevant publications not taken into consideration?**

Please reference the publications in question if applicable.

Response:

C4 **In your view, is the analysis presented accurate, objective and consistent?**

Response:

C5 **The primary aim of this draft justification is to obtain an accurate overview of the published evidence in relation to:**

- **MT practice requirements;**
- **training requirements and skills development of the professionals involved in MT management;**
- **the care pathway of the MT candidate patient.**

In your view, has this aim been achieved?

Response:

C6 **In your view, is the overview of care provision (SIOS data, surveys on regional health boards and professionals) relevant and comprehensive?**

Response:

C7 **In summary, as regards practice requirements, what have you retained in relation to conventional practice in France?**

Response:

C8 **As regards the training and skills requirements for professionals involved in MT therapy, are the guidelines cited consistent with the ongoing reform of post-graduate medical studies?**

In France, which changes need to be envisaged in terms of:

- **basic training;**
- **professional qualification;**
- **skills development?**

Response:

C9 **As regards the pathway of the MT candidate patient, in your view, is the proposed algorithm for the early management of stroke patients in the pre- and intrahospital phase accurate, consistent and relevant?**

Response:

C8 **As regards the pathway of the MT candidate patient, can operational criteria be identified to define stroke service organisation schemes on a regional level?**

Response:

C10 **In your view, are the prospects envisaged, namely MT activity optimisation and assessment, objective and relevant?**

Response:

C11 **Which strategic guidelines are to be applied for the development of care provision based on the regional assessment in terms of:**

- **facility establishment and organisations;**
- **out-of-hours services and continuity of care;**
- **telestroke?**

Response:

LEGIBILITY

L1 **How much time did you need to study the draft assessment justification provided?**

Reading time (in hours):
Any remark(s):

L2 **Did you read the entire justification?**

Response:

L3 **Would you have any suggestions to make to improve the legibility of the**

assessment justification provided?

Response:

REMARKS

Would you like to add any further comments?

R1 *Response:*

Fact sheet

Title	Description
Work method	Appendix to health technology assessment report
Date of on-line publication	July 2018
Date of issue	Only available in electronic format at www.has-sante.fr
Purpose(s)	Assessment of organisational aspects of mechanical thrombectomy in France
Professional(s) concerned	Cf. section 3.3.1
Requested by	Ministry of solidarity and health, Directorate General of Health Care Provision (DGOS)
Sponsor	French National Authority for Health (HAS), Diagnostic and therapeutic procedure assessment department (SEAP)
Project management	Coordination: Huguette LHUILLIER-NKANDJEU, project lead, SEAP (Head of Department: Cédric CARBONNEIL, Assistant Head of Department: Nadia ZEGHARI-SQUALLI). Secretarial duties: Louise TUIL, assistant, SEAP
Participants	External HAS review (assessment report review): "Endovascular mechanical thrombectomy for the treatment of stroke" Ministerial Steering Committee Cf. Section 3.3
Documentary search	October 2010 to October 2017 (documentary search strategy described in appendix 1) with monitoring until April 2018 Conducted by the archivist Emmanuelle BLONDET, assisted by the assistant archivist Maud LEFEVRE, under the responsibility of Frédérique PAGES, Head of Documentation - Monitoring Department, and Christine DEVAUD, Assistant Head of Department
Authors of justification	Huguette LHUILLIER-NKANDJEU, project lead, SEAP, under the responsibility of Nadia ZEGHARI-SQUALLI, Assistant Head of Department, and Cédric CARBONNEIL, Head of Department, SEAP
Approval	Review by the National Committee for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS): June 2018 HAS College: July 2018
Other formats	No formats other than the electronic format available in www.has-sante.fr
Accompanying documents	Framework document, technological assessment report summary, HAS ruling (July 2018), HAS opinion (July 2018) available at www.has-sante.fr

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